



# **Clinical Practice Guideline on the Treatment of Axial Spondyloarthritis and Psoriatic Arthritis**

Supplementary Methodological

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## 1. Introduction

This document contains a brief description of the methodology used to prepare the Clinical Practice Guidelines (CPG) on the Treatment of Axial Spondyloarthritis and Psoriatic Arthritis<sup>1</sup>.

The methodology followed included a series of steps described more extensively in the full CPG version.

## 2. Development methods

A multidisciplinary working group was established composed of health professionals involved in care delivery (rheumatology, dermatology, ophthalmology, gastroenterology and specialized nursing) technical staff of the SER Research Unit and representatives of patients.

An update is warranted, given the time since publication of the previous ESPOGUÍA and the new evidence that has emerged during that time<sup>2,3</sup>. The new scope and objectives were defined by consensus based on the clinical experience and knowledge of the participating health professionals. After establishing the scope and objectives of the guidelines, the members of the GDG set the clinical questions to be answered.

Those questions that addressed the guideline' objectives were selected and rephrased using the Patient-Intervention-Comparison-Outcome (PICO) method. The SPICE (Setting, Perspective, Intervention, Comparison, Evaluation) format was also used to identify qualitative evidence to update the information in the “patient perspective” chapter.

### Clinical Questions update

#### Treatment of Axial Spondyloarthritis

##### Biologic DMARD or JAK inhibitor therapy compared to placebo

In axSpA, what is the efficacy of IL-17 and JAK inhibitors compared to placebo?

##### Predictors of prognosis

In axSpA, what are the predictors of response to IL-17 and JAK inhibitors?

##### Treatment optimisation

In axSpA, can bDMARD therapy be tapered or withdrawn?

##### Extra-musculoskeletal manifestations

In axSpA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)?

##### Obesity and smoking

In axSpA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

## Treatment of psoriatic arthritis

### Treatment with biologic and targeted synthetic disease-modifying antirheumatic drugs

In PsA, what is the efficacy of IL-23 and IL-17 inhibitors and tsDMARDs (JAK inhibitors and apremilast) in treating axial and peripheral disease, enthesitis and dactylitis?

### Treatment with biologic or targeted synthetic disease-modifying antirheumatic drugs compared to TNF inhibitors

In PsA, what is the efficacy, effectiveness and safety of IL-17, IL-23 and JAK inhibitors compared to TNF inhibitors?

### Extra-musculoskeletal manifestations

In PsA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)?

### Obesity and smoking

In PsA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

A literature search was carried out in the following databases: Medline (through PubMed), Embase (Elsevier), Cochrane Library (Wiley Online Library) and the Cumulative Index to Nursing & Allied Health Literature (EBSCOhost). These databases were selected because they are the main sources of biomedical information to which we had access.

In the case of questions for which recommendations remained valid, the literature search was updated using the same strategy as for the 2015 and 2018 ESPOGUÍA CPGs, seeking to retrieve studies published after the previous guidelines, that is, from the beginning of 2015 or 2018 respectively. For the newly developed questions, no restriction was placed on publication date and searches were performed up to the end of August 2023. Initially, all the search strategies were prepared to retrieve only primary studies from the abovementioned databases; however, when this approach yielded few or irrelevant results, it was supplemented by a manual search performed using reference lists of the key documents selected for the review. References proposed by researchers and reviewers consulted were also included. In this way, we identified studies published in 2024, that is, after the initial literature search. Studies included were published in Spanish, English or French.

The references retrieved were managed using EndNote X7.

Regarding the “Patients’ perspective” chapter, an SR was conducted of scientific studies of the experience of patients with Axial Spondyloarthritis or psoriatic arthritis. For this, questions were

formulated using the SPICE framework and, in addition to the aforementioned sources of information, the PsycInfo database was used. Searches were carried out up to April 2019.

The quality of the evidence was assessed by the methods developed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)<sup>4</sup> working group.

**Table 1. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)<sup>4</sup> approach to rating the quality of evidence**

| Quality          | Study design  | Factors that can reduce the quality of the evidence*   | Factors that can increase the quality of the evidence**   |
|------------------|---|--|---|
| High<br>⊕⊕⊕⊕     | RCT<br>--   | <ul style="list-style-type: none"> <li>• Limitations in study quality (design):           <ul style="list-style-type: none"> <li>Large (-1)</li> <li>Very large (-2)</li> </ul> </li> <li>• Inconsistency:           <ul style="list-style-type: none"> <li>Large (-1)</li> <li>Very large (-2)</li> </ul> </li> <li>• Indirectness of evidence:           <ul style="list-style-type: none"> <li>Large (-1)</li> <li>Very large (-2)</li> </ul> </li> <li>• Imprecision:           <ul style="list-style-type: none"> <li>Large (-1)</li> <li>Very large (-2)</li> </ul> </li> <li>• High risk of publication bias: (-1)</li> </ul> | <ul style="list-style-type: none"> <li>Association:           <ul style="list-style-type: none"> <li>• Scientific evidence of a strong association (<math>RR&gt;2</math> or <math>&lt;0.5</math> based on observational studies with no plausible confounders) (+1)</li> <li>• Scientific evidence of a very strong association (<math>RR&gt;5</math> or <math>&lt;0.2</math> based on studies with a low risk of bias) (+2)</li> <li>• Dose-response gradient (+1)</li> <li>• All plausible confounding would reduce the demonstrated effect (+1)</li> </ul> </li> </ul> |
| Moderate<br>⊕⊕⊕⊖ |   |  |   |
| Low ⊕⊕⊖⊖         | Observational studies<br>Studies with other designs |  |   |
| Very low<br>⊕⊖⊖⊖ |   |  |   |

\* In the case of RCTs, the rating of the quality of the scientific evidence may decrease

\*\* In the case of observational studies, the rating of the quality of the evidence may increase

RCT: randomised controlled trial; RR: relative risk.

After the critical reading, the GDG formulated specific recommendations based on the scientific evidence. In the case of the quantitative evidence, the recommendations were based on formal assessment or ‘considered judgement’, after having summarised the evidence for each of the clinical questions. To this end, to aid in the process of moving from evidence to recommendations, the panel used an Evidence to Decision framework that evaluates the following:

- 1) The quality or certainty of the scientific evidence identified
- 2) Patient values and preferences
- 3) The balance between the desirable and undesirable effects of the interventions
- 4) Considerations such as equity, acceptability and feasibility of implementing the interventions
- 5) Other factors.

The direction and strength of the recommendations were also rated using the GRADE system.  
(Table 2).

**Table 2. Implication of the strength of recommendations in the GRADE system<sup>4</sup>**

| Recommendation      | Patients  | Clinicians  | Managers / Policymakers  |
|---------------------|---|---|--|
| Strong              | Most people would agree with the recommended action, and only a small proportion would not. | Most patients should receive the recommended intervention.  | The recommendation can be adopted as a healthcare policy in most situations. |
| Weak or Conditional | The majority of people would agree with the recommended action, but many would not.         | Recognise that different choices will be appropriate for different patients and that you (the doctor) must help each patient make the decision that is most consistent with their values and preferences. | There is a need for considerable debate and the involvement of stakeholders. |

On some occasions, the GDG identified important practical issues it wanted to highlight but related to which there was unlikely to be any supporting evidence. In general, these issues concern aspects of treatment considered good clinical practice and which are not commonly questioned. Such issues have been evaluated as recommendations for good clinical practice. The recommendations associated with the questions from earlier ESPOGUÍA CPGs which were still considered valid have also been transformed from the Oxford Centre for Evidence-based Medicine system for grading recommendations to the GRADE system<sup>5-7</sup>.

Once the previous phases had been completed, an advanced draft of the CPG was produced and this was then reviewed by the working group. Each section of the guideline was analysed, and using a comprehensive approach, any changes considered necessary were proposed.

Subsequently, the guideline was externally reviewed by professionals selected for their knowledge about the disease in question and guideline development methodology.

The draft of the complete version of this CPG was subjected to public scrutiny by members of the SER and other stakeholders (pharmaceutical industry, other scientific societies and patients' associations). For this purpose, it was made available for 15 days on the SER website, with a

form to submit comments, to gather data on people's opinions and scientific assessment of the CPG methodology and/or recommendations.

As well as the SER itself, the following organisations were involved in the development of this guideline, through representation by their members on the GDG: the Spanish Academy of Dermatology and Venereology (AEDV), the Spanish Society of Ophthalmology (SEO), and two patients' associations: Acción Psoriasis and the Coordinator of Spanish Spondyloarthritis Associations (CEADE).

### 3. Literature Search

Between December 2022 and March 2023, a specific systematic search was carried out in the Medline (Pubmed), Embase (Elsevier), and Cochrane Library (Wiley Online Library) databases. Subsequently, an alert service was created for new publications in the electronic databases consulted, which remained active until the closing date of the first complete version of the CPG, in December 2024.

## Treatment of Axial Spondyloarthritis

### Biologic DMARD or JAK inhibitor therapy compared to placebo

#### Clinical question

In axSpA, what is the efficacy of IL-17 and JAK inhibitors compared to placebo?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

#### Medline (Pubmed): 653 resultados

Search: ("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritides"[Title/Abstract:~2]) AND ((("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17\*[Title/Abstract] OR "IL 17\*[Title/Abstract] OR "ixekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR Cosentyx[Title/Abstract] OR "secukinumab"[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract] OR "netakimab"[Supplementary Concept] OR "netakimab"[All Fields] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[All Fields] OR "siliq"[Title/Abstract]) OR ("Janus Kinases"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR tsDMARD\*[Title/Abstract] OR "targeted synthetic

DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR "tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR "upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR Rinfoq[Title/Abstract] OR "GLPG0634"[Supplementary Concept] OR "GLPG0634"[All Fields] OR "filgotinib"[All Fields] OR Jyseleca[Title/Abstract] OR "nilotinib"[Supplementary Concept] OR "nilotinib"[All Fields] OR "tasigna"[Title/Abstract] OR "nilotinib\*"[Title/Abstract])) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type]) Filters: from 2021 - 2023 Sort by: Most Recent

### Embase (Elsevier) 345 resultados

('axial spondyloarthritis'/exp OR 'axspa (spondyloarthritis)':ti,ab OR 'axial spondylarthritis':ti,ab OR 'axial spondyloarthritis':ti,ab OR 'ankylosing spondylitis'/exp OR 'Spondylitis Ankylosis':ti,ab OR 'ankylosing spondylitis':ti,ab OR axSpA:ti,ab OR 'axial SpA':ti,ab OR 'axial spondyloarthritis':ab,ti OR 'non-radiographic axial spondyloarthritis':ti,ab,OR nr-axSpA OR 'axial Ankylosing':ti,ab OR 'Spondylitis rheumatic':ab,ti OR 'Ankylosing Spondylarthritides':ti,ab OR (axial NEAR/3 spondyl\*) OR (axial NEAR/3 Ankylosing\*))

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il-17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn OR netakimab)

OR ('janus kinase'/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti

OR 'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp

690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550'  
OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib'  
OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR

'upadacitinib':exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide tartrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidine 1 carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide tartrate' OR 'abt 494' OR 'abt494' OR 'rinvoq' OR 'upadacitinib' OR 'upadacitinib 2, 3 dihydroxybutanedioate' OR 'upadacitinib hemihydrate' OR 'upadacitinib hydrate' OR 'upadacitinib tartrate' OR

'filgotinib':exp OR 'filgotinib':ti,ab,tn,dn OR 'filgotinib 2 butenedioate':ti,ab,tn,dn OR 'filgotinib hydrochloride':ti,ab,tn,dn OR 'filgotinib maleate':ti,ab,tn,dn OR 'g 146034':ti,ab,tn,dn OR 'g 146034 101':ti,ab,tn,dn OR 'g 146034-101':ti,ab,tn,dn OR 'g146034':ti,ab,tn,dn OR 'g146034 101':ti,ab,tn,dn OR 'g146034-101':ti,ab,tn,dn OR 'glpg 0634':ti,ab,tn,dn OR 'glpg0634':ti,ab,tn,dn OR 'gs 6034':ti,ab,tn,dn OR 'gs6034':ti,ab,tn,dn OR 'jyseleca':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide tartrate' OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2 butenedioate':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2 butenedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'nilotinib':exp OR '4 methyl 3 [ [4 (3 pyridinyl) 2 pyrimidinyl] amino] n [5 (4 methyl 1 imidazolyl) 3 (trifluoromethyl) phenyl] benzamide':ti,ab,tn,dn OR '4 methyl 3 [ [4 (3 pyridinyl) 2 pyrimidinyl] amino] n [5 (4 methyl 1h imidazol 1 yl) 3 (trifluoromethyl) phenyl] benzamide':ti,ab,tn,dn OR '4 methyl n [3 (4 methyl 1h imidazol 1 yl) 5 (trifluoromethyl) phenyl] 3 [4 (pyridin 3 yl) pyrimidin 2 yl] amino] benzamide':ti,ab,tn,dn OR 'amn 107':ti,ab,tn,dn OR 'amn107':ti,ab,tn,dn OR 'nilotinib':ti,ab,tn,dn OR 'nilotinib hydrochloride':ti,ab,tn,dn OR 'nilotinib hydrochloride monohydrate':ti,ab,tn,dn OR 'tasigna':ti,ab,tn,dn))

AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp OR 'cross sectional studies'/exp OR 'observational study'/exp  
OR 'case control studies'/exp OR 'case report'/exp)

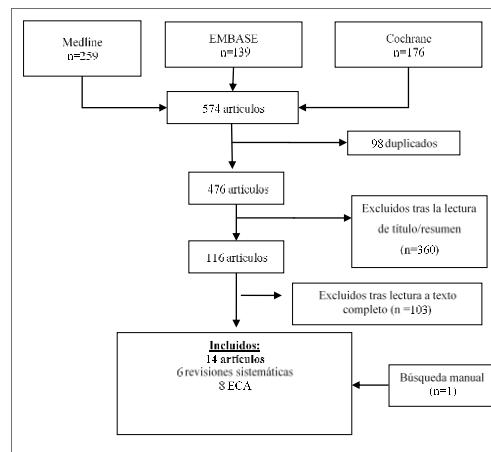
AND [2021-2023]/py

### Cochrane Library 562 resultados

#### ID      Search      Hits

- #1      MeSH descriptor: [Axial Spondyloarthritis] explode all trees      769
- #2      ("Spondylitis Ankylosing" OR "axial SpA" OR "axSpA" OR "Ankylosing Spondylitis" OR "axial spondyloarthritis" OR "axial Ankylosing" OR "non radiographic axial spondyloarthritis" OR nr-axSpA OR axspa OR "Spondylitis rheumatic" OR "Ankylosing Spondylarthritis"):ti,ab,kw      2747
- #3      (axial NEAR/3 spondyl\*):ti,ab,kw OR (axial NEAR/3 Ankylosing\*):ti,ab,kw      786
- #4      #1 OR #2 OR #3 2759
- #5      MeSH descriptor: [Interleukin-17] explode all trees      223
- #6      MeSH descriptor: [Receptors, Interleukin-17] explode all trees      17
- #7      ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR taltz OR "secukinumab" OR 'cosentyx' OR "bimekizumab" OR "netakimab" OR "brodalumab" OR "siliq"):ti,ab,kw      3884
- #8      #5 OR #6 OR #7 3884
- #9      MeSH descriptor: [Janus Kinases] explode all trees      160
- #10     MeSH descriptor: [Janus Kinase Inhibitors] explode all trees      105
- #11     ("janus kinase\*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase\*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD\* OR "targeted synthetic DMARD\*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR "GLPG0634" OR Filgotinib OR Jyseleca OR "nilotinib" OR "tasigna"):ti,ab,kw      4462
- #12     #9 OR #10 OR #11      4470
- #13     #8 OR #12      8167
- #14     #4 AND #13 with Publication Year from 2021 to 2022, in Trials      176

### Diagrama de flujo de los artículos



## Predictors of prognosis

### Clinical question

In axSpA, what are the predictors of response to IL-17 and JAK inhibitors?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA y otros estudios observacionales si no hay ECA (retro y prospectivos).**

### Medline (Pubmed): 449 resultados

("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritis"[Title/Abstract:~2])

AND

(("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17"[Title/Abstract] OR "ilekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR Cosentyx[Title/Abstract] OR "secukinumab"[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract] OR "netakimab"[Supplementary Concept] OR "netakimab"[All Fields] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[All Fields] OR "siliq"[Title/Abstract]))

OR ("Janus Kinases"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR

tsDMARD\*[Title/Abstract] OR "targeted synthetic DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR

"tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR

"upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR Rinvoq[Title/Abstract]

OR "GLPG0634"[Supplementary Concept] OR "GLPG0634"[All Fields] OR "filgotinib"[All Fields] OR Jyseleca[Title/Abstract]

OR "nilotinib"[Supplementary Concept] OR "nilotinib"[All Fields] OR "tasigna"[Title/Abstract] OR "nilotinib\*"[Title/Abstract]))

AND

("gender identity"[MeSH Terms] OR "gender identity"[All Fields] OR "gende\*"[All Fields] OR "sex"[MeSH Terms] OR "sex"[All Fields] OR  
 "Sex Characteristics"[Mesh] OR "Age Factors"[Mesh] OR (sex[tiab] AND characteristic\*[tiab]) OR (age[tiab] AND (factor\*[tiab]))  
 OR "Time Factors"[Mesh] OR "Time Factor\*"[Title/Abstract] OR "longer duration"[Title/Abstract] OR "disease duration"[Title/Abstract] OR "follow up"[Title/Abstract]  
 OR "cigarett\*"[All Fields] OR "cigar\*"[Title/Abstract] OR "snuff"[Title/Abstract] OR "tobacco products"[MeSH Terms] OR "Tobacco Use Disorder"[Mesh] OR "Tobacco Use"[Mesh] OR "tobacco product\*"[All Fields] OR "tobacco"[MeSH Terms] OR "tobacc\*"[Title/Abstract] OR "Smoke"[Mesh] OR "Smokers"[Mesh] OR "smok\*"[Title/Abstract] OR "smoking"[MeSH Terms] OR "Smoke Exposure"[Title/Abstract] OR Vaper[Title/Abstract] OR "Tobacco Use Cessation"[Mesh] OR "nicotine"[Title/Abstract]  
 OR "overweight"[MeSH Terms] OR "overweight\*"[All Fields] OR "body mass"[Title/Abstract] OR "body weight" OR "body mass index"[Title/Abstract] OR BMI[Title/Abstract] OR "body mass index"[MeSH Terms] OR "body mass index obesity"[Text Word] OR "obesity"[MeSH Terms] OR "obese\*"[All Fields] OR "obesit\*"[All Fields]  
 OR "Duration of symptoms"[All Fields]  
 OR "C-Reactive Protein"[Mesh] OR "C Reactive Protein"[Title/Abstract] OR CRP[Title/Abstract]  
 OR "structural damage"[Title/Abstract] OR "Radiographic progression"[Title/Abstract] OR "radiographic damage"[Title/Abstract] OR "Magnetic Resonance Imaging"[All Fields] OR "Magnetic Resonance Imaging"[Mesh] OR "MRI"[Title/Abstract] OR "inflammatory lesion\*"[All Fields]  
 OR "modified Stoke Ankylosing Spondylitis Spine Score"[Title/Abstract] OR "mSASSS"[Title/Abstract]  
 OR "BASRI"[Title/Abstract] OR "Bath Ankylosing Spondylitis Radiology Index"[Title/Abstract] OR "New York criteria"[Title/Abstract]  
 OR "anti inflammatory agents non steroidal"[Pharmacological Action] OR "anti inflammatory agents, non steroidal"[MeSH Terms] OR "non-steroidal anti-inflammatory agent\*"[Title/Abstract] OR NSAID\*[Title/Abstract] OR "naproxen"[MeSH Terms] OR "naproxen\*"[All Fields] OR "naproxene"[All Fields] OR "ibuprofen"[MeSH Terms] OR "ibuprofen\*"[All Fields] OR "ibuprofen s"[All Fields] OR "ibuprofens"[All Fields] OR "diclofenac"[MeSH Terms] OR "diclofenac\*"[All Fields] OR "diclofenac\*"[MeSH Terms] OR "diclofenac\*"[All Fields] OR "diclophenac\*"[All Fields] OR "etoricoxib\*"[MeSH Terms] OR "etoricoxib\*"[All Fields]  
 OR "HLA-B27 Antigen"[Mesh] OR "HLAB27" OR HLA-B27 OR "Biomarkers"[Mesh] OR "Biomarker\*"[Title/Abstract] OR "Treatment Outcome"[Mesh] OR "Treatment Failure"[Mesh] OR "treatment failure\*"[All Fields] OR "treatment respons\*"[All Fields])  
 NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))

NOT ("Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type])

Embase (Elsevier): 305 resultados

('axial spondyloarthritis'/exp OR 'axspa (spondyloarthritis)':ti,ab OR 'axial spondylarthritis':ti,ab OR 'axial spondyloarthritis':ti,ab OR 'ankylosing spondylitis'/exp OR 'Spondylitis Ankylosis':ti,ab OR 'ankylosing spondylitis':ti,ab OR axSpA:ti,ab OR 'axial SpA':ti,ab OR 'axial spondyloarthritis':ab,ti OR 'non-radiographic axial spondyloarthritis':ti,ab,OR nr-axSpA OR 'axial Ankylosing':ti,ab OR 'Spondylitis rheumatic':ab,ti OR 'Ankylosing Spondylarthritides':ti,ab OR (axial NEAR/3 spondyl\*) OR (axial NEAR/3 Ankylosing\*))

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn OR 'netakimab'/exp OR 'netakimab':ti,ab,kw)

OR ('janus kinase'/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti

OR 'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp 690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550' OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib' OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR

'upadacitinib'/exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1

pyrrolidinecarboxamide tartrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide tartrate' OR 'abt 494' OR 'abt494' OR 'rinfoq' OR 'upadacitinib' OR 'upadacitinib 2, 3 dihydroxybutanedioate' OR 'upadacitinib hemihydrate' OR 'upadacitinib hydrate' OR 'upadacitinib tartrate' OR  
 'filgotinib'/exp OR 'filgotinib':ti,ab,tn,dn OR 'filgotinib 2 butenedioate':ti,ab,tn,dn OR 'filgotinib hydrochloride':ti,ab,tn,dn OR 'filgotinib maleate':ti,ab,tn,dn OR 'g 146034':ti,ab,tn,dn OR 'g 146034 101':ti,ab,tn,dn OR 'g 146034-101':ti,ab,tn,dn OR 'g146034':ti,ab,tn,dn OR 'g146034 101':ti,ab,tn,dn OR 'g146034-101':ti,ab,tn,dn OR 'glpg 0634':ti,ab,tn,dn OR 'glpg0634':ti,ab,tn,dn OR 'gs 6034':ti,ab,tn,dn OR 'gs6034':ti,ab,tn,dn OR 'jyseleca':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2 butenedioate':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2 butenedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'nilotinib'/exp OR '4 methyl 3 [ [4 (3 pyridinyl) 2 pyrimidinyl] amino] n [5 (4 methyl 1 imidazolyl) 3 (trifluoromethyl) phenyl] benzamide':ti,ab,tn,dn OR '4 methyl 3 [ [4 (pyridin 3 yl) pyrimidin 2 yl] amino] n [5 (4 methyl 1h imidazol 1 yl) 3 (trifluoromethyl) phenyl] benzamide':ti,ab,tn,dn OR '4 methyl n [3 (4 methyl 1 imidazolyl) 5 (trifluoromethyl) phenyl] 3 [4 (3 pyridinyl) 2 pyrimidinylamino] benzamide':ti,ab,tn,dn OR '4 methyl n [3 (4 methyl 1h imidazol 1 yl) 5 (trifluoromethyl) phenyl] 3 [4 (pyridin 3 yl) pyrimidin 2 yl] benzamide':ti,ab,tn,dn OR 'amn 107':ti,ab,tn,dn OR 'amn107':ti,ab,tn,dn OR 'nilotinib':ti,ab,tn,dn OR 'nilotinib hydrochloride':ti,ab,tn,dn OR 'nilotinib hydrochloride monohydrate':ti,ab,tn,dn OR 'tasigna':ti,ab,tn,dn))  
 AND  
 ('gender identity'/exp OR 'gender identity':ti,ab,kw OR 'gender self-identification':ti,ab,kw OR 'identity, sexual':ti,ab,kw OR 'sex identification':ti,ab,kw OR 'sexual identification':ti,ab,kw OR 'sexual identity':ti,ab,kw OR 'sexual self-identification':ti,ab,kw OR 'sex'/exp OR sex:ti,ab  
 OR 'sex characteristics'/exp OR 'sex characteristic\*':ab,ti OR 'age factors'/exp OR 'age factor\*':ab,ti OR gender:ab,ti  
 OR 'time factor'/exp OR 'time factor\*':ti,ab,kw OR 'disease duration'/exp OR 'disease duration':ab,ti OR "longer duration":ab,ti OR 'follow up':ab,ti  
 OR "cigarette\*":ab,ti OR "cigar\*":ab,ti OR "snuff":ab,ti OR 'snuff'/exp OR 'tobacco products'/exp OR "tobacco products":ab,ti OR 'tobacco use disorder'/exp OR "Tobacco Use

Disorder\*":ab,ti OR 'tobacco use'/exp OR "Tobacco Use":ab,ti OR "tobacco product\*":ab,ti OR 'tobacco'/exp OR 'tobac\*':ab,ti OR 'smoke'/exp OR "Smokers":ab,ti OR "smok\*":ab,ti OR 'smoking'/exp OR 'smoke exposure'/exp OR "Smoke Exposure":ab,ti OR Vaper:ab,ti OR 'tobacco use cessation'/exp OR "Tobacco Use Cessation":ab,ti OR 'nicotine'/exp OR "nicotine":ab,ti OR  
 'obesity'/exp OR 'adipose tissue hyperplasia':ti,ab,kw OR 'adipositas':ti,ab,kw OR 'adiposity':ti,ab,kw OR 'alimentary obesity':ti,ab,kw OR 'body weight':ti,ab,kw OR 'corpulence':ti,ab,kw OR 'fat overload syndrome':ti,ab,kw OR 'nutritional obesity':ti,ab,kw OR 'obes\*':ti,ab,kw OR 'obesit\*':ti,ab,kw OR 'overweight\*':ti,ab,kw OR 'body mass'/exp OR 'bmi':ti,ab,kw OR 'quetelet index':ti,ab,kw OR 'body ban mass':ti,ab,kw OR 'body mass':ti,ab,kw OR 'body mass index':ti,ab,kw  
 OR "Duration of symptom\*s":ab,ti  
 OR 'c reactive protein'/exp OR 'C reactive protein':ab,ti OR 'crp'/exp OR crp:ab,ti  
 OR 'structural damage':ab,ti OR 'radiographic progression':ab,ti OR 'radiographic damage':ab,ti OR 'magnetic resonance imaging'/exp OR 'magnetic resonance imaging':ab,ti OR 'mri'/exp OR 'mri':ab,ti OR "inflammatory lesion\*":ab,ti  
 OR 'modified stoke ankylosing spondylitis spine score':ab,ti OR 'msasss':ab,ti OR 'basri':ab,ti OR 'bath ankylosing spondylitis radiology index':ab,ti OR 'new york criteria':ab,ti  
 OR 'nonsteroid antiinflammatory agent'/exp OR "non-steroidal anti-inflammatory agent\*":ti,ab,kw OR 'nsaid':ti,ab,kw OR 'anti inflammatory agents, non steroidal':ti,ab,kw OR 'anti-inflammatory agents, non-steroidal':ti,ab,kw OR 'antiinflammatory agent, nonsteroid':ti,ab,kw OR 'non steroid antiinflammatory agent':ti,ab,kw OR 'non steroid antiinflammatory drug':ti,ab,kw OR 'non steroid anti inflammatory agent':ti,ab,kw OR 'non steroid antiinflammatory drug':ti,ab,kw OR 'nonsteroid antiinflammatory agent':ti,ab,kw OR 'nonsteroid antiinflammatory drug':ti,ab,kw OR 'nonsteroid antirheumatic agent':ti,ab,kw OR 'nonsteroidal anti inflammatory drug':ti,ab,kw OR 'nonsteroidal antiinflammatory drug':ti,ab,kw OR 'nonsteroidal anti-inflammatory drugs':ti,ab,kw OR 'nonsteroidal antiinflammatory agent':ti,ab,kw OR 'nonsteroidal antiinflammatory drug':ti,ab,kw  
 OR 'naproxen'/exp OR '2 (6 methoxy 2 naphthyl) propionic acid':ti,ab,kw OR '2 (6 methoxynaphthalen 2 yl) propanoic acid':ti,ab,kw OR '2 (6` methoxy 2` naphthyl) propionic acid':ti,ab,kw OR '2 naphthaleneacetic acid, 6 methoxy alpha methyl':ti,ab,kw OR '4flex puregel':ti,ab,kw OR '6 methoxy alpha methyl 2 naphthaleneacetic acid':ti,ab,kw OR 'actromadol':ti,ab,kw OR 'acusprain':ti,ab,kw OR 'aflamax':ti,ab,kw OR 'aflaxen':ti,ab,kw OR 'agilex':ti,ab,kw OR 'agilxen':ti,ab,kw OR 'aleve':ti,ab,kw OR 'aleve classic':ti,ab,kw OR 'aleve feminax':ti,ab,kw OR 'aleve intense':ti,ab,kw OR 'aleve select':ti,ab,kw OR 'alevetabs':ti,ab,kw OR 'alpoxen':ti,ab,kw OR 'alpron':ti,ab,kw OR 'analgesin dolo':ti,ab,kw OR 'anapran':ti,ab,kw OR 'anaprox':ti,ab,kw OR 'anaprox ds':ti,ab,kw OR 'anaprox-ds':ti,ab,kw OR 'anexopen':ti,ab,kw OR 'antalgin (naproxen)':ti,ab,kw OR 'apo-napro':ti,ab,kw OR 'apo-naproxen':ti,ab,kw OR 'apranax':ti,ab,kw OR 'apranax dolo':ti,ab,kw OR 'apraxin':ti,ab,kw OR 'apronax':ti,ab,kw OR 'artagen':ti,ab,kw OR 'arthrosin ec':ti,ab,kw OR 'artron':ti,ab,kw OR 'artroxen':ti,ab,kw OR 'axer alfa':ti,ab,kw OR 'babel':ti,ab,kw OR 'bay 117031':ti,ab,kw OR 'bay117031':ti,ab,kw OR 'bayh 6689':ti,ab,kw OR 'bayh6689':ti,ab,kw OR 'bipronyl':ti,ab,kw OR 'bonyl':ti,ab,kw OR 'congex':ti,ab,kw OR 'crysanal':ti,ab,kw OR 'dafloxaen':ti,ab,kw OR 'daprox':ti,ab,kw OR 'daprox'

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OR 'ibuprofen'/exp OR '2 (4 isobutylphenyl) propionic acid':ti,ab,kw OR '2 (para isobutylphenyl) propionic acid':ti,ab,kw OR '2 [4 (2 methylpropyl) phenyl] propionic acid':ti,ab,kw OR 'abfen':ti,ab,kw OR 'abidol (ibuprofen)':ti,ab,kw OR 'aches-n-pain':ti,ab,kw OR 'act-3':ti,ab,kw OR 'actiprofen':ti,ab,kw OR 'adagin':ti,ab,kw OR 'adagin forte':ti,ab,kw OR 'adex 200':ti,ab,kw OR 'adex liqui-gels':ti,ab,kw OR 'adolorin ibuforte':ti,ab,kw OR 'adolorini direkt':ti,ab,kw OR 'advil':ti,ab,kw OR 'advil infantil':ti,ab,kw OR 'advil liqui-gels':ti,ab,kw OR 'advil liquid caps':ti,ab,kw OR 'advil liquifast':ti,ab,kw OR 'advil liquigel':ti,ab,kw OR 'advil migraine liqui-gels':ti,ab,kw OR 'advil mono':ti,ab,kw OR 'advil paediatric':ti,ab,kw OR 'advil pediatric':ti,ab,kw OR 'advil reliva forte':ti,ab,kw OR 'advil ultra':ti,ab,kw OR 'advil ultra forte':ti,ab,kw OR

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OR 'diclofenac'/exp OR '2 (2, 6 dichloroanilino) phenylacetic acid':ti,ab,kw OR '2 (2, 6 dichlorophenylamino) phenylacetic acid':ti,ab,kw OR '2 [ (2, 6 dichlorophenyl) amino] benzeneacetic acid':ti,ab,kw OR '2 [2 [ (2, 6 dichlorophenyl) amino] phenyl] acetic acid':ti,ab,kw OR 'abdiflam':ti,ab,kw OR 'abitren':ti,ab,kw OR 'acuflam':ti,ab,kw OR 'akis':ti,ab,kw OR 'algipatch':ti,ab,kw OR 'algistick':ti,ab,kw OR 'algopain eze':ti,ab,kw OR 'algoplast':ti,ab,kw OR 'allvoran':ti,ab,kw OR 'almiral':ti,ab,kw OR 'almiral gel':ti,ab,kw OR 'almiral sr':ti,ab,kw OR 'alonpin':ti,ab,kw OR 'amz 001':ti,ab,kw OR 'amz001':ti,ab,kw OR 'antalcalm':ti,ab,kw OR 'apo-diclofenac ec':ti,ab,kw OR 'arcanafenac':ti,ab,kw OR 'arthrif'en':ti,ab,kw OR 'artren':ti,ab,kw OR 'artrenac':ti,ab,kw OR 'artrites':ti,ab,kw OR 'artrites retard':ti,ab,kw OR 'assaren':ti,ab,kw OR 'athrofen':ti,ab,kw OR 'ba 47210':ti,ab,kw OR 'ba47210':ti,ab,kw OR 'batafil':ti,ab,kw OR 'berafen gel':ti,ab,kw OR 'berifen':ti,ab,kw OR 'berifen gel':ti,ab,kw OR 'betaren':ti,ab,kw OR 'bolabomin':ti,ab,kw OR 'calozan':ti,ab,kw OR 'catanac':ti,ab,kw OR 'catas':ti,ab,kw OR 'cencenag':ti,ab,kw OR 'clo-far':ti,ab,kw OR 'clofec':ti,ab,kw OR 'clofen':ti,ab,kw OR 'clonac':ti,ab,kw OR 'clonaren':ti,ab,kw OR 'clonodifen':ti,ab,kw OR 'cordralan':ti,ab,kw OR 'curinflam':ti,ab,kw OR 'ddl plaster':ti,ab,kw OR 'declophen':ti,ab,kw OR 'decrol':ti,ab,kw OR 'deflam-k':ti,ab,kw OR 'deflamat':ti,ab,kw OR 'delimon (diclofenac)':ti,ab,kw OR 'delphinac':ti,ab,kw OR 'denaclof':ti,ab,kw OR 'depain':ti,ab,kw OR 'depain plaster':ti,ab,kw OR 'dic 075v':ti,ab,kw OR 'dic075v':ti,ab,kw OR 'diceus':ti,ab,kw OR 'dicipan':ti,ab,kw OR 'diclac':ti,ab,kw OR 'diclac duo':ti,ab,kw OR 'diclax':ti,ab,kw OR 'diclax sr':ti,ab,kw OR 'diclo':ti,ab,kw OR 'diclo basan':ti,ab,kw OR 'diclo divido':ti,ab,kw OR 'diclo divido long':ti,ab,kw OR 'diclo puren':ti,ab,kw OR 'diclo recip':ti,ab,kw OR 'diclo-basan':ti,ab,kw OR 'diclobasan':ti,ab,kw OR 'diclobene':ti,ab,kw OR 'diclod':ti,ab,kw OR 'diclodent':ti,ab,kw OR 'diclodoc':ti,ab,kw OR 'diclodolor':ti,ab,kw OR 'diclofen':ti,ab,kw OR 'diclofen cremogel':ti,ab,kw OR 'diclofenac':ti,ab,kw OR 'diclofenac rekur':ti,ab,kw OR 'diclofenac resin':ti,ab,kw OR 'diclofenac resinate':ti,ab,kw OR 'diclofenac sodium':ti,ab,kw OR 'dicloflam':ti,ab,kw OR 'diclohexal':ti,ab,kw OR 'dicloin':ti,ab,kw OR 'diclomax':ti,ab,kw OR 'diclomol':ti,ab,kw OR 'diclon':ti,ab,kw OR 'diclopax':ti,ab,kw OR 'diclophenac sodium':ti,ab,kw OR 'diclopuren':ti,ab,kw OR 'dicloral':ti,ab,kw OR 'dicloran gel':ti,ab,kw OR 'diclorecep':ti,ab,kw OR 'dicloren':ti,ab,kw OR 'diclorem':ti,ab,kw OR 'diclosan sr':ti,ab,kw OR 'diclosian':ti,ab,kw OR 'diclotec':ti,ab,kw OR 'diclowal':ti,ab,kw OR 'dicsnal':ti,ab,kw OR 'dif'en':ti,ab,kw OR 'difena':ti,ab,kw OR 'difenac':ti,ab,kw OR 'difenol gel':ti,ab,kw OR 'difnal k':ti,ab,kw OR 'dioxaflex':ti,ab,kw OR 'dioxaflex retard':ti,ab,kw OR 'divoltar':ti,ab,kw OR 'dixol':ti,ab,kw OR 'dixol forte':ti,ab,kw OR 'doflastad':ti,ab,kw OR 'doflex':ti,ab,kw OR 'dolare':ti,ab,kw OR 'dolaut gel':ti,ab,kw OR 'dolflam-retard':ti,ab,kw OR 'dolo voltaren':ti,ab,kw OR 'doloflam':ti,ab,kw OR 'dolotren':ti,ab,kw OR 'dolotren gel':ti,ab,kw OR 'dolotren retard':ti,ab,kw OR 'doragon':ti,ab,kw OR 'dosanac':ti,ab,kw OR 'duravolten':ti,ab,kw OR 'dycon sr':ti,ab,kw OR 'dyloject':ti,ab,kw OR 'ecofenac':ti,ab,kw OR 'econac':ti,ab,kw OR 'effekton':ti,ab,kw OR 'effekton retard':ti,ab,kw OR 'eflagen':ti,ab,kw OR 'epifenac':ti,ab,kw OR 'eslofen':ti,ab,kw OR 'evadol':ti,ab,kw OR 'evinopon':ti,ab,kw OR 'feloran':ti,ab,kw OR 'fenac':ti,ab,kw OR 'fenadium':ti,ab,kw OR 'fenaspec':ti,ab,kw OR 'flameril':ti,ab,kw OR 'flexagen':ti,ab,kw OR 'flogofenac':ti,ab,kw OR 'flogosin d':ti,ab,kw OR 'flogozan':ti,ab,kw OR 'fortfen sr':ti,ab,kw OR 'freejex':ti,ab,kw OR 'glimbax (diclofenac)':ti,ab,kw OR 'gp 45840':ti,ab,kw OR 'grofenac':ti,ab,kw OR 'hizemin':ti,ab,kw OR 'imflac':ti,ab,kw OR 'inac gel':ti,ab,kw OR 'indicam':ti,ab,kw OR 'inflamac':ti,ab,kw OR 'inflanac':ti,ab,kw OR 'inforce (drug)':ti,ab,kw OR 'isv 205':ti,ab,kw OR 'isv205':ti,ab,kw OR 'jonac gel':ti,ab,kw OR

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OR 'etoricoxib'/exp OR '5 chloro 2 (2 methyl 5 pyridyl) 3 (4 methylsulfonylphenyl) pyridine':ti,ab,kw OR '5 chloro 3 [4 (methylsulfonyl) phenyl] 2 (6 methylpyridin 3 yl) pyridine':ti,ab,kw OR '5 chloro 6` methyl 3 [4 (methylsulfonyl) phenyl] 2, 3` bipyridine':ti,ab,kw OR 'acoxxel':ti,ab,kw OR 'algix':ti,ab,kw OR 'arcoxia':ti,ab,kw OR 'auxib':ti,ab,kw OR 'bericox':ti,ab,kw OR 'caretor':ti,ab,kw OR 'coxerit':ti,ab,kw OR 'coxeta':ti,ab,kw OR 'coxient':ti,ab,kw OR 'coxiloc':ti,ab,kw OR 'coxitor':ti,ab,kw OR 'coxolin':ti,ab,kw OR 'doloxib':ti,ab,kw OR 'ecoxyton':ti,ab,kw OR 'etori':ti,ab,kw OR 'etoriax':ti,ab,kw OR 'etorican':ti,ab,kw OR 'etoricox':ti,ab,kw OR 'etoricoxib':ti,ab,kw OR 'etoricoxib hydrochloride':ti,ab,kw OR 'etorikoksib':ti,ab,kw OR 'etorilin':ti,ab,kw OR 'etoxib':ti,ab,kw OR 'evetore':ti,ab,kw OR 'exinef':ti,ab,kw OR 'exxiv':ti,ab,kw OR 'hallitztolva':ti,ab,kw OR 'imesol':ti,ab,kw OR 'itoroxx':ti,ab,kw OR 'kostarox':ti,ab,kw OR 'I 791456':ti,ab,kw OR 'I791456':ti,ab,kw OR 'linzavo':ti,ab,kw OR 'mk 0663':ti,ab,kw OR 'mk 663':ti,ab,kw OR

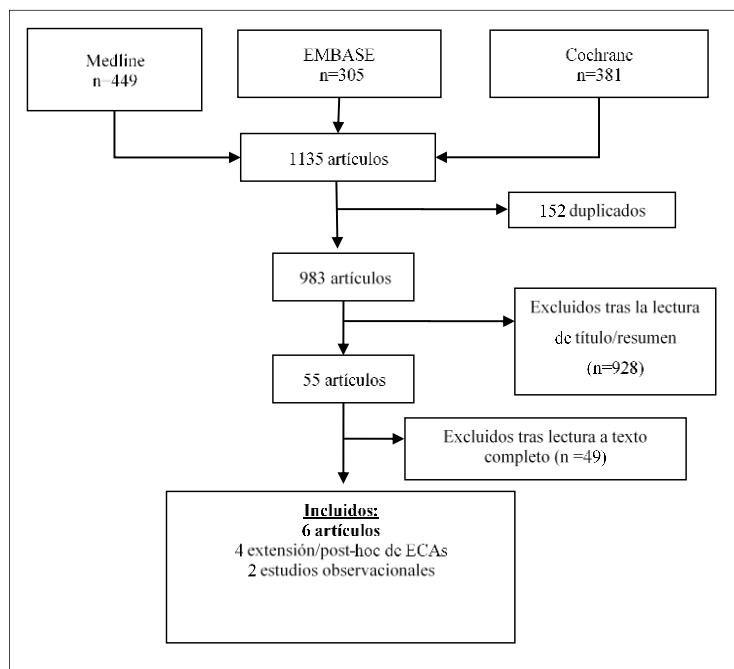
'mk0663':ti,ab,kw OR 'mk663':ti,ab,kw OR 'narox (etoricoxib)':ti,ab,kw OR 'nucoxia':ti,ab,kw OR 'oxidraxib':ti,ab,kw OR 'roticox':ti,ab,kw OR 'tauxib':ti,ab,kw OR 'turox':ti,ab,kw  
 OR 'hla b27 antigen':exp OR 'hl a 27b antigen':ti,ab,kw OR 'hl a b27':ti,ab,kw OR 'hla b27 antigen':ti,ab,kw OR 'antigen b 27':ti,ab,kw OR 'antigen hla 27b':ti,ab,kw OR 'hla 27b antigen':ti,ab,kw OR 'hla b27':ti,ab,kw OR 'hla-b27 antigen':ti,ab,kw OR 'human lymphocyte antigen 27b':ti,ab,kw OR "HLAB27" OR HLA-B27 OR  
 'biological marker':exp OR 'biological marker':ti,ab,kw OR 'biological markers':ti,ab,kw OR 'biomarker':ti,ab,kw OR 'biomarkers':ti,ab,kw OR 'marker, biological':ti,ab,kw OR 'treatment outcome':exp OR 'health care outcome and process assessment':ti,ab,kw OR 'healthcare outcome and process assessment':ti,ab,kw OR 'medical futility':ti,ab,kw OR 'outcome and process assessment (health care)':ti,ab,kw OR 'outcome and process assessment, health care':ti,ab,kw OR 'outcome management':ti,ab,kw OR 'patient outcome':ti,ab,kw OR 'therapeutic outcome':ti,ab,kw OR 'therapy outcome':ti,ab,kw OR 'treatment outcome':ti,ab,kw OR 'treatment failure':exp OR 'lack of therapeutic efficacy':ti,ab,kw OR 'therapy failure':ti,ab,kw OR 'treatment failure':ti,ab,kw OR "treatment respons\*":ab,ti)  
 AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
 NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
 'consensus development'/exp OR 'cross sectional studies'/exp OR 'observational study'/exp  
 OR 'case control studies'/exp OR 'case report'/exp)

### Cochrane Library: 381 resultados

| ID  | Search  | Hits |
|-----|---|------|
| #1  | MeSH descriptor: [Axial Spondyloarthritis] explode all trees  | 835  |
| #2  | ("Spondylitis Ankylosing" OR "axial SpA" OR "axSpA" OR "Ankylosing Spondylitis" OR "axial spondyloarthritis" OR "axial Ankylosing" OR "non radiographic axial spondyloarthritis" OR nr-axSpA OR axspa OR "Spondylitis rheumatic" OR "Ankylosing Spondylarthritides"):ti,ab,kw   | 2810 |
| #3  | (axial NEAR/3 spondyl*):ti,ab,kw OR (axial NEAR/3 Ankylosing*):ti,ab,kw   | 820  |
| #4  | #1 OR #2 OR #3  | 2823 |
| #5  | MeSH descriptor: [Interleukin-17] explode all trees   | 256  |
| #6  | MeSH descriptor: [Receptors, Interleukin-17] explode all trees  | 19   |
| #7  | ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR taltz OR "secukinumab" OR 'cosentyx' OR "bimekizumab" OR "netakimab" OR "brodalumab" OR "siliq"):ti,ab,kw  | 3985 |
| #8  | #5 OR #6 OR #7  | 3985 |
| #9  | MeSH descriptor: [Janus Kinases] explode all trees  | 201  |
| #10 | MeSH descriptor: [Janus Kinase Inhibitors] explode all trees  | 141  |
| #11 | ("janus kinase*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD* OR "targeted synthetic DMARD*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR "GLPG0634" OR Filgotinib OR Jysleeca OR "nilotinib" OR "tasigna"):ti,ab,kw | 4596 |
| #12 | #9 OR #10 OR #11  | 4610 |
| #13 | #8 OR #12   | 8402 |
| #14 | #4 AND #13  | 593  |

- #15 MeSH descriptor: [Gender Identity] explode all trees 334
- #16 MeSH descriptor: [Sex] explode all trees 37
- #17 MeSH descriptor: [Sex Characteristics] explode all trees 1466
- #18 MeSH descriptor: [Age Factors] explode all trees 12287
- #19 MeSH descriptor: [Time Factors] explode all trees 72996
- #20 ("gende\*" OR sex OR "Time Factor\*" OR "longer duration" OR "disease duration" OR "follow up" OR "cigarette\*" OR "cigar\*" OR "snuff" OR "tobacc\*" OR Smok\* OR Vaper OR "nicotine"):ti,ab 308650
- #21 ((sex AND characteristic\*) OR (age AND factor\*)):ti,ab 57181
- #22 MeSH descriptor: [Tobacco Products] explode all trees 646
- #23 MeSH descriptor: [Tobacco Use Disorder] explode all trees 2016
- #24 MeSH descriptor: [Tobacco Use] explode all trees 506
- #25 MeSH descriptor: [Tobacco] explode all trees 286
- #26 MeSH descriptor: [Smoke] explode all trees 524
- #27 MeSH descriptor: [Smokers] explode all trees 658
- #28 MeSH descriptor: [Obesity] explode all trees 18204
- #29 ("overweight\*" OR "body mass" OR "body weight" OR BMI OR "obese\*" OR "obesit\*" OR "Duration of symptom\*" OR "C Reactive Protein" OR CRP OR "structural damage" OR "Radiographic progression" OR "radiographic damage" OR "Magnetic Resonance Imaging" OR "MRI" OR "inflammatory lesion\*" OR "modified Stoke Ankylosing Spondylitis Spine Score" OR mSASSS OR BASRI OR "Bath Ankylosing Spondylitis Radiology Index" OR "New York criteri\*"):ti,ab 176355
- #30 MeSH descriptor: [C-Reactive Protein] explode all trees 5519
- #31 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees 10648
- #32 ("non-steroidal anti-inflammatory agent\*" OR NSAID\* OR "naproxen\*" OR "ibuprofen" OR "diclofenac\*" OR "diclophenac\*" OR "etoricoxib"):ti,ab 17903
- #33 MeSH descriptor: [HLA-B27 Antigen] explode all trees 22
- #34 MeSH descriptor: [Biomarkers] explode all trees 26628
- #35 MeSH descriptor: [Treatment Outcome] explode all trees 174018
- #36 ("HLAB27" OR HLA-B27 OR "Biomarker\*" OR "Treatment Outcom\*" OR "treatment failure\*" OR "treatment respons\*"):ti,ab 21912
- #37 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 667569
- #38 #14 AND #37 381

### Diagrama de flujo de los artículos



## Treatment optimisation

### Clinical question

In axSpA, can bDMARD therapy be tapered or withdrawn?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

### Medline (Pubmed): 1099 resultados

("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritis"[Title/Abstract:~2]))

AND

((("interrupt\*"[Title/Abstract] OR discontin\*[Title/Abstract] OR disruption\*[Title/Abstract] OR termination[Title/Abstract] OR remove[Title/Abstract] OR "cut off" [Title/Abstract] OR cessation[Title/Abstract] OR suspend\*[Title/Abstract] OR discontinuation[Title/Abstract] OR discontinued[Title/Abstract] OR withdrawal[Title/Abstract] OR withdraw[Title/Abstract] OR withdr\*[Title/Abstract] OR stop[Title/Abstract] OR stopping[Title/Abstract] OR titration[Title/Abstract] OR withhold\*[Title/Abstract]))

OR

("drug tapering"[MeSH Terms] OR "drug tapering"[All Fields] OR "Tapering\*"[Title/Abstract] OR "remission"[Title/Abstract] OR "Remission Induction"[Mesh] OR "drug-free remission"[Title/Abstract] OR "decrease dose"[Title/Abstract] OR "dose-reduction"[Title/Abstract] OR "Dosing down"[Title/Abstract] OR "dose-adjustment"[Title/Abstract] OR "reduction"[Title/Abstract] OR "administration and dosage"[Subheading] OR "Dose-Response Relationship, Drug"[Mesh] OR "Drug Administration Schedule"[Mesh] OR "optimization"[Title/Abstract] OR "optimizing"[Title/Abstract] OR "de escalation"[Title/Abstract] OR "Dose Reduction"[Title/Abstract] OR "Dose Reductions"[Title/Abstract] OR "Reduction Dose"[Title/Abstract] OR "Reductions Dose"[Title/Abstract] OR "Dose Tapering"[Title/Abstract] OR "Tapering Dose"[Title/Abstract] OR "Drug Dosage Calculations"[Mesh] OR discont\*[Title/Abstract] OR discontinue[Title/Abstract] OR taper[Title/Abstract]))

OR ("increase"[Title/Abstract] OR "increased"[Title/Abstract] OR "increas\*"[Title/Abstract] OR "increasing\*"[Title/Abstract] OR Augmentation[Title/Abstract] OR raise[Title/Abstract] OR "dosage adjustment\*"[Title/Abstract] OR "Treatment holiday"[Title/Abstract] OR "Drug withdrawal"[Title/Abstract] OR "Variable dosing"[Title/Abstract] OR "Flexible

dosing"[Title/Abstract] OR "Dose adjustment"[Title/Abstract] OR "Disease flare"[Title/Abstract] OR "Stepwise"[Title/Abstract] OR "decreas\*" [Title/Abstract] OR "On-demand treatment"[Title/Abstract] OR lowering[Title/Abstract] OR decreasing[Title/Abstract] OR Lessening[Title/Abstract] OR diminution[Title/Abstract] OR deprescription[Title/Abstract] OR spacing[Title/Abstract] OR "Recurrence"[Mesh] OR "Withholding Treatment"[Mesh:NoExp] OR intensification\*[Title/Abstract] OR lengthening[Title/Abstract]))

AND

((("Receptors, Tumor Necrosis Factor"[Mesh] OR "Antibodies, Monoclonal"[Mesh] OR "Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh] OR "tumor necrosis factor-alpha antagonists"[Title/Abstract] OR "tumor necrosis factor-alpha inhibitor\*" [Title/Abstract] OR "anti-tumor necrosis factor-alpha"[Title/Abstract] OR "anti-tumor necrosis factor agent"[All Fields] OR "anti-tnf alpha"[Title/Abstract] OR "anti-TNF"[Title/Abstract] OR "anti-tumor necrosis factor alpha"[Title/Abstract] OR "anti TNF alpha"[Title/Abstract] OR "TNF alpha inhibitor\*" [Title/Abstract]

OR "infliximab"[Mesh] OR infliximab[Title/Abstract] OR remicade[Title/Abstract] OR avakine[All Fields] OR

"Etanercept"[Mesh] OR etanercept[All Fields] OR enbrel[All Fields] OR tunex[All Fields] OR

"adalimumab"[Mesh] OR adalimumab[Title/Abstract] OR humira[All Fields] OR

"certolizumab pegol"[Mesh] OR certolizumab[All Fields] OR cimzia[Title/Abstract] OR

"golimumab"[Supplementary Concept] OR golimumab[All Fields] OR simponi[All Fields]) OR

("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*" [Title/Abstract] OR "IL-17 blocker\*" [Title/Abstract] OR "IL-17"[Title/Abstract] OR "ilekizumab"[Supplementary Concept] OR "ilekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR Cosentyx[Title/Abstract] OR "secukinumab"[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract]))

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))

NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type])

### Embase (Elsevier): 660 resultados

('axial spondyloarthritis')/exp OR 'axspa (spondyloarthritis)':ti,ab OR 'axial spondylarthritis':ti,ab OR 'axial spondyloarthritis':ti,ab OR 'ankylosing spondylitis')/exp OR 'Spondylitis Ankylosing':ti,ab OR 'ankylosing spondylitis':ti,ab OR axSpA:ti,ab OR 'axial SpA':ti,ab OR 'axial spondyloarthritis':ab,ti OR 'non-radiographic axial spondyloarthritis':ti,ab OR nr-

axSpA OR 'axial Ankylosing':ti,ab OR 'Spondylitis rheumatic':ab,ti OR 'Ankylosing Spondylarthritides':ti,ab OR (axial NEAR/3 spondyl\*) OR (axial NEAR/3 Ankylosing\*))

AND

('interrupt\*':ti,ab,kw OR discontin\*:ti,ab,kw OR disruption\*:ti,ab,kw OR termination:ti,ab,kw OR remove:ti,ab,kw OR 'cut off':ti,ab,kw OR cessation:ti,ab,kw OR suspend\*:ti,ab,kw OR discontinuation:ti,ab,kw OR discontinued:ti,ab,kw OR withdrawal:ti,ab,kw OR withdraw:ti,ab,kw OR withdr\*:ti,ab,kw OR stop:ti,ab,kw OR stopping:ti,ab,kw OR titration:ti,ab,kw OR withhold\*:ti,ab,kw OR 'drug tapering':ti,ab,kw OR 'tapering\*':ti,ab,kw OR 'remission':ti,ab,kw OR 'drug-free remission':ti,ab,kw OR 'decrease dose':ti,ab,kw OR 'dosing down':ti,ab,kw OR 'dose-adjustment':ti,ab,kw OR 'reduction':ti,ab,kw OR 'optimization':ti,ab,kw OR 'optimizing':ti,ab,kw OR 'de escalation':ti,ab,kw OR 'dose reduction':ti,ab,kw OR 'dose reductions':ti,ab,kw OR 'reduction dose':ti,ab,kw OR 'reductions dose':ti,ab,kw OR 'dose tapering':ti,ab,kw OR 'tapering dose':ti,ab,kw OR discont\*:ti,ab,kw OR discontinue:ti,ab,kw OR taper:ti,ab,kw OR 'increase':ti,ab,kw OR 'increased':ti,ab,kw OR 'increas\*':ti,ab,kw OR 'increasing\*':ti,ab,kw OR augmentation:ti,ab,kw OR raise:ti,ab,kw OR 'dosage adjustment\*':ti,ab,kw OR 'treatment holiday':ti,ab,kw OR 'drug withdrawal':ti,ab,kw OR 'variable dosing':ti,ab,kw OR 'flexible dosing':ti,ab,kw OR 'dose adjustment':ti,ab,kw OR 'disease flare':ti,ab,kw OR 'stepwise':ti,ab,kw OR 'decreas\*':ti,ab,kw OR 'on-demand treatment':ti,ab,kw OR lowering:ti,ab,kw OR decreasing:ti,ab,kw OR lessening:ti,ab,kw OR diminution:ti,ab,kw OR deprescription:ti,ab,kw OR spacing:ti,ab,kw OR intensification\*:ti,ab,kw OR lengthening:ti,ab,kw OR 'remission/exp OR 'disease regression':ti,ab,kw OR 'disease remission':ti,ab,kw OR 'regression, disease':ti,ab,kw OR 'remission':ti,ab,kw OR 'remission induction':ti,ab,kw OR 'remission rate':ti,ab,kw OR 'remission, spontaneous':ti,ab,kw OR 'spontaneous regression':ti,ab,kw OR 'spontaneous remission':ti,ab,kw

OR 'drug dose reduction/exp OR 'dosage decrease':ti,ab,kw OR 'dosage reduction':ti,ab,kw OR 'dose decrease':ti,ab,kw OR 'dose reduction':ti,ab,kw OR 'drug dose reduction':ti,ab,kw OR 'drug tapering':ti,ab,kw OR 'reduction of drug dosage':ti,ab,kw OR 'reduction of drug dose':ti,ab,kw OR 'reduction, drug dose':ti,ab,kw

OR 'dose response/exp OR 'dosage effect relation':ti,ab,kw OR 'dose activity relation':ti,ab,kw OR 'dose activity relationship':ti,ab,kw OR 'dose dependence':ti,ab,kw OR 'dose effect':ti,ab,kw OR 'dose effect curve':ti,ab,kw OR 'dose effect relation':ti,ab,kw OR 'dose effect relationship':ti,ab,kw OR 'dose rate effect':ti,ab,kw OR 'dose response':ti,ab,kw OR 'dose response (drug)':ti,ab,kw OR 'dose response curve':ti,ab,kw OR 'dose response relation':ti,ab,kw OR 'dose response relationship':ti,ab,kw OR 'dose response study':ti,ab,kw OR 'dose-response relationship, drug':ti,ab,kw OR 'dose-response relationship, immunologic':ti,ab,kw OR 'drug dosage scheme':ti,ab,kw OR 'drug dose dependence':ti,ab,kw OR 'drug dose effect':ti,ab,kw OR 'drug dose effect relation':ti,ab,kw OR 'drug dose effect relationship':ti,ab,kw OR 'drug dose response':ti,ab,kw OR 'drug dose response curve':ti,ab,kw OR 'drug dose response relation':ti,ab,kw OR 'drug response relation':ti,ab,kw

OR 'drug administration/exp OR 'administration, drug':ti,ab,kw OR 'drug administration':ti,ab,kw

OR 'dose calculation/exp OR 'calculation, dosage':ti,ab,kw OR 'dosage calculation':ti,ab,kw OR 'dose calculation':ti,ab,kw OR 'dose finding':ti,ab,kw OR 'drug dosage calculation':ti,ab,kw OR

'drug dosage calculations':ti,ab,kw OR 'drug dose calculation':ti,ab,kw OR 'drug dose calculations':ti,ab,kw

OR 'treatment withdrawal':exp OR 'treatment withdrawal':ti,ab,kw OR 'withdrawal, treatment':ti,ab,kw OR 'withholding treatment':ti,ab,kw OR recurrence:ti,ab,kw)

AND

(('interleukin 17':exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab':exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab':exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'bimekizumab':exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn)

OR

('tumor necrosis factor receptor':exp OR 'tumor necrosis factor':exp OR 'monoclonal antibody':exp OR 'tnf alfa' OR 'tnf alpha' OR 'human recombinant tumour necrosis factor alpha' OR 'tissue necrosis factor' OR 'tumor necrosis factor' OR 'tumor necrosis factor alfa' OR 'tumor necrosis factor alpha' OR 'tumor necrosis factor-alpha' OR 'tumor necrosis factors' OR 'tumor necrosis serum' OR 'tumour necrosis factor' OR 'tumour necrosis factor alfa' OR 'tumour necrosis factor alpha' OR 'tumour necrosis factor-alpha' OR 'tumour necrosis factors' OR 'tumour necrosis serum' OR 'anti-tumor necrosis factor agent':ab,ti OR 'tumor necrosis factor-alpha antagonists':ti,ab OR 'tumor necrosis factor-alpha inhibitor\*':ti,ab OR "anti-tumor necrosis factor-alpha":ab,ti OR "anti-TNF":ab,ti OR "anti-tumor necrosis factor alpha":ab,ti OR "anti TNF":ab,ti OR 'anti TNF alpha':ti,ab OR "TNF alpha inhibitor\*":ab,ti OR 'infliximab':exp OR infliximab:ab,ti OR remicade:ab,ti OR avakine:ab,ti OR 'etanercept':exp OR etanercept:ab,ti OR enbrel:ab,ti OR tunex:ab,ti OR 'adalimumab':exp OR adalimumab:ab,ti OR humira:ab,ti OR 'certolizumab pegol':exp OR 'cdp 870':ab,ti OR 'cdp870':ab,ti OR 'certolizumab':ab,ti OR 'cimzia':ab,ti OR 'golimumab':exp OR 'cnto 148':ab,ti OR 'cnto148':ab,ti OR 'golimumab':ab,ti OR 'simponi':ab,ti))

AND [embase]/lim NOT [medline]/lim NOT ('animal':exp NOT ('animal':exp AND 'human':exp)) NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR 'consensus development':exp OR 'cross sectional studies':exp OR 'observational study':exp OR 'case control studies':exp OR 'case report':exp)

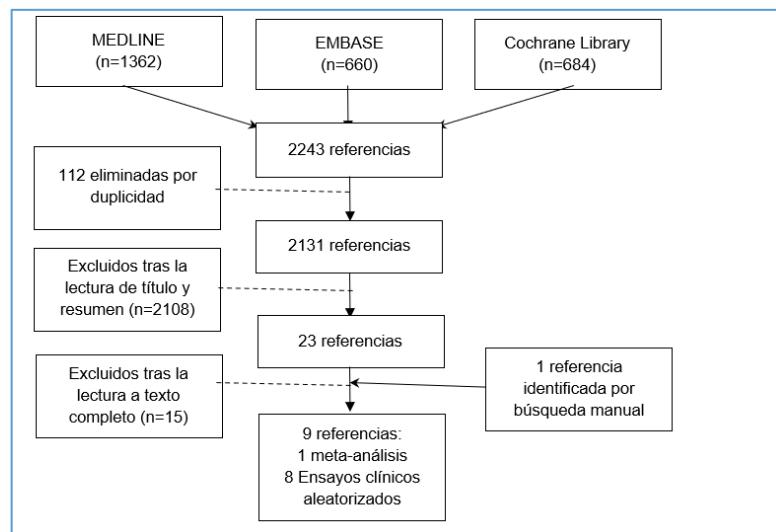
### Cochrane Library: 684 resultados

ID      Search Hits

- |    |  |     |
|----|--|-----|
| #1 | MeSH descriptor: [Axial Spondyloarthritis] explode all trees   | 769 |
| #2 | ("Spondylitis Ankylosing" OR "axial SpA" OR "axSpA" OR "Ankylosing Spondylitis" OR "axial spondyloarthritis" OR "axial Ankylosing" OR "non radiographic axial spondyloarthritis" |     |

OR nr-axSpA OR axspa OR "Spondylitis rheumatic" OR "Ankylosing Spondylarthritides"):ti,ab,kw 2754  
#3 (axial NEAR/3 spondyl\*):ti,ab,kw OR (axial NEAR/3 Ankylosing\*):ti,ab,kw 790  
#4 #1 OR #2 OR #3 2766  
#5 MeSH descriptor: [Interleukin-17] explode all trees 223  
#6 MeSH descriptor: [Receptors, Interleukin-17] explode all trees 17  
#7 ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR taltz OR "secukinumab" OR 'cosentyx' OR "bimekizumab"):ti,ab,kw 3809  
#8 #5 OR #6 OR #7 3809  
#9 MeSH descriptor: [Receptors, Tumor Necrosis Factor] explode all trees 1366  
#10 MeSH descriptor: [Antibodies, Monoclonal] explode all trees 16088  
#11 MeSH descriptor: [Tumor Necrosis Factor-alpha] explode all trees 3333  
#12 ("tumor necrosis factor-alpha antagonists" OR "tumor necrosis factor-alpha inhibitor\*" OR "anti-tumor necrosis factor-alpha" OR "anti-tnf alpha" OR "anti-TNF" OR "anti-tumor necrosis factor alpha" OR "anti TNF alpha" OR "TNF alpha inhibitor\*"):ab,ti,kw 997  
#13 MeSH descriptor: [Infliximab] explode all trees 802  
#14 MeSH descriptor: [Etanercept] explode all trees 811  
#15 MeSH descriptor: [Adalimumab] explode all trees 885  
#16 MeSH descriptor: [Certolizumab Pegol] explode all trees 187  
#17 (infliximab OR remicade OR avakine OR etanercept OR enbrel OR tunex OR adalimumab OR humira OR certolizumab OR cimzia golimumab OR simponi):ti,ab,kw 7913  
#18 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 25380  
#19 #8 OR #18 28325  
#20 #4 AND #19 1295  
#21 MeSH descriptor: [Remission Induction] explode all trees 4209  
#22 MeSH descriptor: [Drug Tapering] explode all trees 27  
#23 MeSH descriptor: [Dose-Response Relationship, Drug] explode all trees 31230  
#24 MeSH descriptor: [Drug Administration Schedule] explode all trees 24468  
#25 MeSH descriptor: [Drug Dosage Calculations] explode all trees 234  
#26 MeSH descriptor: [Withholding Treatment] explode all trees 439  
#27 MeSH descriptor: [Recurrence] explode all trees 12919  
#28 ("interrupt\*" OR discontin\* OR disruption\* OR termination OR remove OR "cut off" OR cessation OR suspend\* OR discontinuation OR discontinued OR withdrawal OR withdraw OR withdr\* OR stop OR stopping OR titration OR withhold\* OR "drug tapering" OR "Tapering\*" OR "dose reduction" OR "remission" OR "drug-free remission" OR "decrease dose" OR "dose reduction" OR "Dosing down" OR "dose-adjustment" OR "reduction" OR "optimization" OR "optimizing" OR "de escalation" OR "Dose Reduction" OR "Dose Reductions" OR "Reduction Dose" OR "Reductions Dose" OR "Dose Tapering" OR "Tapering Dose" OR discont\* OR discontinue OR taper OR "increase" OR "increased" OR "increas\*" OR "increasing\*" OR Augmentation OR raise OR "dosage adjustment\*" OR "Treatment holiday" OR "Drug withdrawal" OR "Variable dosing" OR "Flexible dosing" OR "Dose adjustment" OR "Disease flare" OR "Stepwise" OR "decreas\*" OR "On-demand treatment" OR lowering OR decreasing OR Lessening OR diminution OR deprescription OR spacing OR intensification\* OR lengthening ):ti,ab,kw 699375  
#29 #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 728576  
#30 #20 AND #29 684

### Diagrama de flujo de los artículos



## Extra-musculoskeletal manifestations

### Clinical question

In axSpA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

### Medline (Pubmed): 1099 resultados

("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritis"[Title/Abstract:~2])

AND

(("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17"[Title/Abstract] OR "IL 17"[Title/Abstract] OR "ixekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[Title/Abstract] OR "secukinumab"[Title/Abstract] OR cosentyx[Title/Abstract] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[Title/Abstract] OR lumicef[Title/Abstract] OR siliq[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract] OR "bimzelx"[Title/Abstract]))

OR

("Interleukin-23"[Mesh] OR "interleukin-23"[Title/Abstract] OR "Interleukin 23"[Title/Abstract] OR "IL-23"[Title/Abstract] OR "IL 23"[Title/Abstract] OR "risankizumab"[Supplementary Concept] OR "risankizumab"[Title/Abstract] OR skyrizi[Title/Abstract] OR "guselkumab"[Supplementary Concept] OR "guselkumab"[Title/Abstract] OR tremfya[Title/Abstract] OR "tildrakizumab"[Supplementary Concept] OR "tildrakizumab"[Title/Abstract] OR ilumetri[Title/Abstract] OR ilumya[Title/Abstract]))

OR ("APY0201" [Supplementary Concept] OR "Interleukin 12-23"[Title/Abstract] OR "IL-12-23"[Title/Abstract] OR "interleukin-12-23"[Title/Abstract] OR "IL-12-23 inhibitor\*"[Title/Abstract] OR "IL 12-23"[Title/Abstract] OR "IL 12,23"[Title/Abstract] OR "IL 12/23"[Title/Abstract] OR "Ustekinumab"[Mesh] OR "Ustekinumab"[Title/Abstract] OR Stelara[Title/Abstract] OR Abatacept)

OR ("Janus Kinases"[Mesh] OR "Janus Kinase Inhibitors"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR "janus tyrosine kinase"[Title/Abstract] OR "protein tyrosine kinase janus"[Title/Abstract] OR tsDMARD\*[Title/Abstract] OR "targeted synthetic DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR  
 "tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR  
 "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR  
 "upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR  
 Rinvog[Title/Abstract] OR "GLPG0634"[Supplementary Concept] OR "GLPG0634"[All Fields] OR  
 "filgotinib"[All Fields] OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[All Fields] OR "apremilast"[Supplementary Concept] OR "apremilast"[All Fields])

OR

("Receptors, Tumor Necrosis Factor"[Mesh] OR "Antibodies, Monoclonal"[Mesh] OR "Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh] OR "tumor necrosis factor-alpha antagonists"[Title/Abstract] OR "tumor necrosis factor-alpha inhibitor\*"[Title/Abstract] OR "anti-tumor necrosis factor-alpha"[Title/Abstract] OR "anti-tumor necrosis factor agent"[All Fields] OR "anti-tnf alpha"[Title/Abstract] OR "anti-TNF"[Title/Abstract] OR "anti-tumor necrosis factor alpha"[Title/Abstract] OR "anti TNF alpha"[Title/Abstract] OR "TNF alpha inhibitor\*"[Title/Abstract])

OR "infliximab"[Mesh] OR infliximab[Title/Abstract] OR remicade[Title/Abstract] OR avakine[All Fields] OR

"Etanercept"[Mesh] OR etanercept[All Fields] OR enbrel[All Fields] OR tunex[All Fields] OR  
 "adalimumab"[Mesh] OR adalimumab[Title/Abstract] OR humira[All Fields] OR  
 "certolizumab pegol"[Mesh] OR certolizumab[All Fields] OR cimzia[Title/Abstract] OR  
 "golimumab"[Supplementary Concept] OR golimumab[All Fields] OR simponi[All Fields]))

AND

("uveitis"[MeSH Terms] OR "uveitis"[All Fields] OR "uveitides"[All Fields] OR uveitis OR  
 "psoriasis"[MeSH Terms] OR "psoriasis"[Title/Abstract] OR "psoriases"[Title/Abstract] OR  
 "psoria\*"[Title/Abstract] OR "psoriatic\*"[Title/Abstract] OR IBD[Title/Abstract] OR  
 "inflammatory bowel diseases"[MeSH Terms] OR "inflammatory bowel diseases"[All Fields] OR  
 "inflammatory bowel disease"[All Fields])

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))

NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR  
 "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical  
 Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development  
 Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published  
 Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type])

("Uveitis, Anterior"[Mesh] OR "Iritis"[Mesh] OR Iriti\*[Title/Abstract] OR  
 iridocyclitis\*[Title/Abstract] OR "behcet syndrome"[MeSH Terms] OR "behcet"[All Fields] OR

"behcet syndrome"[All Fields] OR Behcet's[Title/Abstract] OR Behcet\*[Title/Abstract] OR behcet[All Fields] OR "behcet s"[All Fields] OR "behcets"[All Fields] OR "Uveitis anterior"[Title/Abstract] OR "anterior Uveitis"[Title/Abstract] OR (Uveitis AND (anterior OR "HLA-B27 Antigen"[Mesh] OR "HLA-B27"[Title/Abstract] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract] OR "Ankylosing Spondylitis"[Title/Abstract] OR "Sarcoidosis"[Mesh] OR "Sarcoidosis"[Title/Abstract] OR "Tubulointerstitial nephritis and uveitis"[Supplementary Concept] OR TINU[Title/Abstract]))

### Embase (Elsevier): 621 resultados

('Arthritis, Psoriatic'/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab)

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn) OR

('interleukin 23'/exp OR IL-23:ti,ab OR 'il 23':ti,ab OR 'interleukin 23':ti,ab OR 'interleukin-23':ti,ab OR 'risankizumab'/exp OR 'abbv 066':ti,ab,tn,dn OR 'abbv066':ti,ab,tn,dn OR 'bi 655066':ti,ab,tn,dn OR 'bi655066':ti,ab,tn,dn OR 'risankizumab':ti,ab,tn,dn OR 'risankizumab rzaa':ti,ab,tn,dn OR 'risankizumab-rzaa':ti,ab,tn,dn OR 'skyrizi':ti,ab,tn,dn OR 'guselkumab'/exp OR 'cnto 1959':ti,ab,kw OR 'cnto1959':ti,ab,kw OR 'guselkumab':ti,ab,kw OR 'tremfya':ti,ab,kw OR 'tildrakizumab'/exp OR 'ilumetri':ti,ab,tn,dn OR 'ilumya':ti,ab,tn,dn OR 'mk 3222':ti,ab,tn,dn OR 'mk3222':ti,ab,tn,dn OR 'sch 900222':ti,ab,tn,dn OR 'sch900222':ti,ab,tn,dn OR 'sunpg 1622':ti,ab,tn,dn OR 'sunpg1622':ti,ab,tn,dn OR 'sunpg 1623':ti,ab,tn,dn OR 'sunpg1623':ti,ab,tn,dn OR 'tildrakizumab':ti,ab,tn,dn OR 'tildrakizumab asmn':ti,ab,tn,dn OR 'tildrakizumab-asmn':ti,ab,tn,dn)

OR ('janus kinase'/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti OR

'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp 690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550' OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib' OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR  
  
'upadacitinib'/exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide tartrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide tartrate' OR 'abt 494' OR 'abt494' OR 'rinvog' OR 'upadacitinib' OR 'upadacitinib 2, 3 dihydroxybutanedioate' OR 'upadacitinib hemihydrate' OR 'upadacitinib hydrate' OR 'upadacitinib tartrate' OR

'deucravacitinib'/exp OR '6 (cyclopropanecarbonylamino) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropanecarbonylamino) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl)

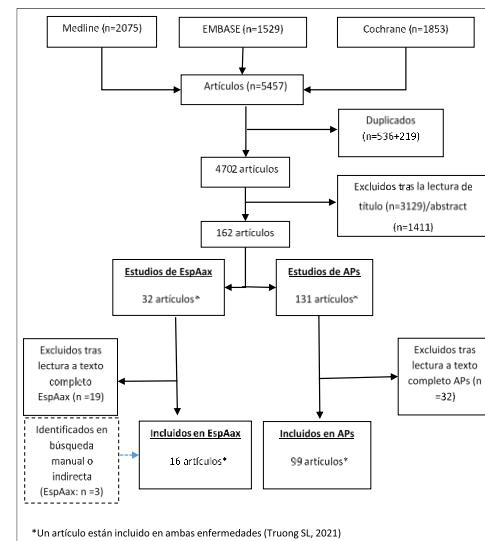


## Cochrane Library: 1411 resultados

### ID      Search Hits

- #1      MeSH descriptor: [Arthritis, Psoriatic] explode all trees 542
- #2      ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath\*" OR "Arthropathy psoria\*" OR "arthritis psoriatica" OR "Psoriatic rheumatism" OR "arthritis psoriatica"):ti,ab,kw 2738
- #3      (arthritis NEAR/3 "Psoria\*"):ti,ab,kw OR (Psoria\* NEAR/3 arthritis):ti,ab,kw 2826
- #4      #1 OR #2 OR #3 2829
- #5      MeSH descriptor: [Interleukin-17] explode all trees 223
- #6      MeSH descriptor: [Receptors, Interleukin-17] explode all trees 17
- #7      ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR "secukinumab" OR 'cosentyx' OR "brodalumab" OR "bimekizumab"):ti,ab,kw 3882
- #8      #5 OR #6 OR #7 3882
- #9      MeSH descriptor: [Interleukin-23] explode all trees 109
- #10     ("interleukin-23" OR "Interleukin 23" OR "IL-23" OR "IL 23" OR "risankizumab" OR "guselkumab" OR "tildrakizumab") 6059
- #11     #9 OR #10 6073
- #12     MeSH descriptor: [Janus Kinases] explode all trees 160
- #13     MeSH descriptor: [Janus Kinase Inhibitors] explode all trees 105
- #14     ("janus kinase\*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase\*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD\* OR "targeted synthetic DMARD\*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR "GLPG0634" OR "filgotinib" OR deucravacitinib OR apremilast):ti,ab,kw 4554
- #15     #12 OR #13 OR #14 4560
- #16     #8 OR #11 OR #15 12839
- #17     #4 AND #16 1411

## Diagrama de flujo de los artículos



## Obesity and smoking

### Clinical question

In axSpA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

**En cuanto al diseño de estudios se han considerado para su inclusión: subanálisis de ensayos clínicos, cohortes de expuestos vs. no expuestos, casos y controles.**

### Medline (Pubmed): 1397 resultados

(("Arthritis, Psoriatic"[Mesh] OR "Arthritis Psoriatic"[Title/Abstract] OR "Arthritic Psoriasis"[Title/Abstract] OR "psoriatic arthritis"[Title/Abstract] OR "psoriasis arthritis"[Title/Abstract] OR "psoriatic arthropath\*[Title/Abstract] OR "Arthropathy psoria\*"[Title/Abstract] OR "arthritis psoriatica"[Title/Abstract] OR "Psoriatic rheumatism"[Title/Abstract]) OR ("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritides"[Title/Abstract:~2]))

AND

(("cigarett\*"[All Fields] OR "cigar\*"[Title/Abstract] OR "snuff"[Title/Abstract] OR "tobacco products"[MeSH Terms] OR "Tobacco Use Disorder"[Mesh] OR "Tobacco Use"[Mesh] OR "tobacco product\*"[All Fields] OR "tobacco"[MeSH Terms] OR "tobacc\*"[Title/Abstract] OR "Smoke"[Mesh] OR "Smokers"[Mesh] OR "smok\*"[Title/Abstract] OR "smoking"[MeSH Terms] OR "Smoke Exposure"[Title/Abstract] OR Vaper[Title/Abstract] OR "Tobacco Use Cessation"[Mesh] OR "nicotine"[Title/Abstract]))

OR

("overweight"[MeSH Terms] OR "overweight\*"[All Fields] OR "body mass"[Title/Abstract] OR "body weight"[Title/Abstract] OR "body mass index"[Title/Abstract] OR BMI[Title/Abstract] OR "body mass index"[MeSH Terms] OR "body Weight"[Title/Abstract] OR "obesity"[MeSH Terms] OR "obese\*"[All Fields] OR "obesit\*"[All Fields]))

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))

NOT ("Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type]))

### Embase (Elsevier): 2277 resultados

(('Arthritis, Psoriatic')/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab) OR ('axial spondyloarthritis'/exp OR 'axspa (spondyloarthritis)':ti,ab OR 'axial spondylarthritis':ti,ab OR 'axial spondyloarthritis':ti,ab OR 'ankylosing spondylitis'/exp OR 'Spondylitis Ankylosing':ti,ab OR 'ankylosing spondylitis':ti,ab OR axSpA:ti,ab OR 'axial SpA':ti,ab OR 'axial spondyloarthritis':ab,ti OR 'non-radiographic axial spondyloarthritis':ti,ab OR nr-axSpA OR 'axial Ankylosing':ti,ab OR 'Spondylitis rheumatic':ab,ti OR 'Ankylosing Spondylarthritides':ti,ab OR (axial NEAR/3 spondyl\*) OR (axial NEAR/3 Ankylosing\*)))

AND

('cigarette smoking')/exp OR 'cigarette smoker':ti,ab,kw OR 'cigarette smoking':ti,ab,kw OR 'smoking, cigarette':ti,ab,kw OR 'cigarette'/exp OR 'cigarette\*':ti,ab,kw OR "cigar\*" OR 'filter cigarette':ti,ab,kw OR 'tobacco snuff'/exp OR 'snuff':ti,ab,kw OR 'snuff tobacco':ti,ab,kw OR 'tobacco snuff':ti,ab,kw OR 'tobacco use'/exp OR 'tobacco usage':ti,ab,kw OR 'tobacco use':ti,ab,kw OR "tobacco product\*":ti,ab,kw OR  
 'tobacco dependence'/exp OR 'dependence, tobacco':ti,ab,kw OR 'nicotine abuse':ti,ab,kw OR 'nicotine addiction':ti,ab,kw OR 'nicotine dependence':ti,ab,kw OR 'nicotine dependency':ti,ab,kw OR 'nicotinism':ti,ab,kw OR 'tobacco abuse':ti,ab,kw OR 'tobacco addiction':ti,ab,kw OR 'tobacco dependence':ti,ab,kw OR 'tobacco dependency':ti,ab,kw OR 'tobacco use disorder':ti,ab,kw OR 'tobaccoism':ti,ab,kw OR 'tobacco'/exp OR 'condensate, tobacco':ti,ab,kw OR 'tobacc\*':ti,ab,kw OR 'tobacco condensate':ti,ab,kw OR 'tobacco constituent':ti,ab,kw OR 'tobacco product':ti,ab,kw OR 'tobacco products':ti,ab,kw OR 'tobacco smoke condensate':ti,ab,kw OR 'tobacco smoke extract':ti,ab,kw OR 'tobacco smoke residue':ti,ab,kw OR 'smoke'/exp OR 'smok\*':ti,ab,kw OR 'smoking'/exp OR 'behavior, smoking':ti,ab,kw OR 'behaviour, smoking':ti,ab,kw OR 'reverse smoking':ti,ab,kw OR 'smoker':ti,ab,kw OR 'smokers':ti,ab,kw OR 'smoking':ti,ab,kw OR 'smoking behavior':ti,ab,kw OR 'smoking behaviour':ti,ab,kw OR 'tobacco smoking':ti,ab,kw OR 'smoke exposure'/exp OR 'smoking cessation'/exp OR 'abstination, smoking':ti,ab,kw OR 'abstinence from nicotine':ti,ab,kw OR 'abstinence from smoking':ti,ab,kw OR 'abstinence from tobacco':ti,ab,kw OR 'cessation, smoking':ti,ab,kw OR 'dehabituation, smoking':ti,ab,kw OR 'nicotine abstinence':ti,ab,kw OR 'nicotine abstinence':ti,ab,kw OR 'nicotine cessation':ti,ab,kw OR 'nicotine withdrawal':ti,ab,kw OR 'quit smoking':ti,ab,kw OR 'smoking abstinence':ti,ab,kw OR 'smoking cessation':ti,ab,kw OR 'smoking dehabituation':ti,ab,kw OR 'smoking, stopping':ti,ab,kw OR 'stop smoking':ti,ab,kw OR 'stopping smoking':ti,ab,kw OR 'tobacco use cessation':ti,ab,kw OR 'nicotine'/exp OR nicotine:ti,ab,kw OR Vaper:ti,ab,kw

OR

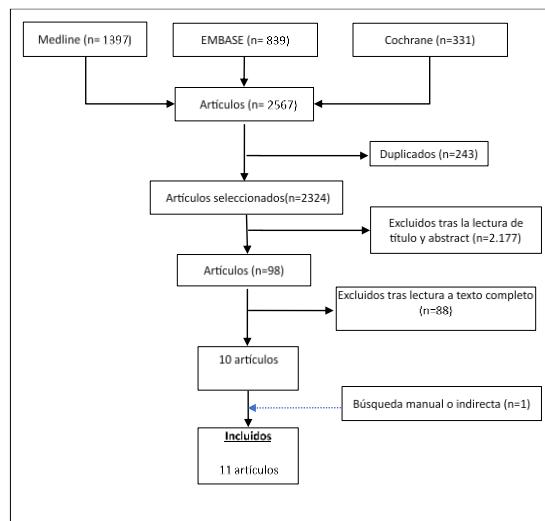
'body mass')/exp OR 'bmi':ti,ab,kw OR 'quetelet index':ti,ab,kw OR 'body ban mass':ti,ab,kw OR 'body mass':ti,ab,kw OR 'body mass index':ti,ab,kw OR 'body weight'/exp OR 'body weight':ti,ab,kw OR 'total body weight':ti,ab,kw OR 'weight, body':ti,ab,kw OR 'obesity'/exp OR 'adipose tissue hyperplasia':ti,ab,kw OR 'adipositas':ti,ab,kw OR 'adiposity':ti,ab,kw OR 'alimentary obesity':ti,ab,kw OR 'body weight, excess':ti,ab,kw OR 'corpulence':ti,ab,kw OR 'fat

overload syndrome':ti,ab,kw OR 'nutritional obesity':ti,ab,kw OR 'obesitas':ti,ab,kw OR 'obesit\*':ti,ab,kw OR "obese\*":ti,ab,kw OR 'overweight\*':ti,ab,kw)  
AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp)

### Cochrane Library: 331 resultados

| ID  | Search  | Hits   |
|-----|---|--------|
| #1  | MeSH descriptor: [Axial Spondyloarthritis] explode all trees  | 835    |
| #2  | ("Spondylitis Ankylosing" OR "axial SpA" OR "axSpA" OR "Ankylosing Spondylitis" OR "axial spondyloarthritis" OR "axial Ankylosing" OR "non radiographic axial spondyloarthritis" OR nr-axSpA OR axspa OR "Spondylitis rheumatic" OR "Ankylosing Spondylarthritides"):ti,ab,kw | 2810   |
| #3  | (axial NEAR/3 spondyl*):ti,ab,kw OR (axial NEAR/3 Ankylosing*):ti,ab,kw   | 820    |
| #4  | MeSH descriptor: [Arthritis, Psoriatic] explode all trees   | 628    |
| #5  | ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath*" OR "Arthropathy psoria*" OR "arthritis psoriatica" OR "Psoriatic rheumatism" OR "arthritis psoriatica"):ti,ab,kw                                 | 2809   |
| #6  | (arthritis NEAR/3 "Psoria*") :ti,ab,kw OR (Psoria* NEAR/3 arthritis):ti,ab,kw   | 2899   |
| #7  | #1 OR #2 OR #3 OR #4 OR #5 OR #6  | 5258   |
| #8  | MeSH descriptor: [Tobacco Products] explode all trees   | 646    |
| #9  | MeSH descriptor: [Tobacco Use Disorder] explode all trees   | 2016   |
| #10 | MeSH descriptor: [Tobacco Use] explode all trees  | 506    |
| #11 | MeSH descriptor: [Tobacco] explode all trees  | 286    |
| #12 | MeSH descriptor: [Tobacco Use Cessation] explode all trees  | 153    |
| #13 | MeSH descriptor: [Smoke] explode all trees  | 524    |
| #14 | MeSH descriptor: [Smokers] explode all trees  | 658    |
| #15 | MeSH descriptor: [Smoke] explode all trees  | 524    |
| #16 | MeSH descriptor: [Obesity] explode all trees  | 18204  |
| #17 | MeSH descriptor: [Overweight] explode all trees   | 21526  |
| #18 | MeSH descriptor: [Body Mass Index] explode all trees  | 12344  |
| #19 | ("cigarett*" OR "cigar*" OR "snuff" OR "tobacco product*" OR "tobacc*" OR "smok*" OR "Smoke Exposure" OR Vaper OR "nicotine"):ti,ab,kw  | 8739   |
| #20 | ("overweight*" OR "body mass" OR "body weight" OR BMI OR "obese*" OR "obesit*"):ti,ab,kw  | 140113 |
| #21 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20   | 152787 |
| #22 | #7 AND #21  | 331    |

### Diagrama de flujo de los artículos



## Treatment of psoriatic arthritis

### Treatment with biologic and targeted synthetic disease-modifying antirheumatic drugs

#### Clinical question

In PsA, what is the efficacy of IL-23 and IL-17 inhibitors and tsDMARDs (JAK inhibitors and apremilast) in treating axial and peripheral disease, enthesitis and dactylitis?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

#### Medline (Pubmed): 1307 resultados

("Arthritis, Psoriatic"[Mesh] OR "Arthritis Psoriatic"[Title/Abstract] OR "Arthritic Psoriasis"[Title/Abstract] OR "psoriatic arthritis"[Title/Abstract] OR "psoriatic arthropath\*"[Title/Abstract] OR "Arthropathy psoria\*"[Title/Abstract] OR "psoriasis arthritis"[Title/Abstract] OR "arthritis psoriatica"[Title/Abstract] OR "Psoriatic rheumatism"[Title/Abstract])

AND

((("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17"[Title/Abstract] OR "IL 17"[Title/Abstract] OR "ixekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[Title/Abstract] OR cosentyx[Title/Abstract] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[Title/Abstract] OR lumicef[Title/Abstract] OR siliq[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract] OR bimzelx[Title/Abstract]))

OR

("Interleukin-23"[Mesh] OR "interleukin-23"[Title/Abstract] OR "Interleukin 23"[Title/Abstract] OR "IL-23"[Title/Abstract] OR "IL 23"[Title/Abstract] OR "risankizumab"[Supplementary Concept] OR "risankizumab"[Title/Abstract] OR skyrizi[Title/Abstract] OR "guselkumab"[Supplementary Concept] OR "guselkumab"[Title/Abstract] OR tremfya[Title/Abstract] OR "tildrakizumab"[Supplementary Concept] OR "tildrakizumab"[Title/Abstract] OR ilumetri[Title/Abstract] OR ilumya[Title/Abstract]))

OR ("Janus Kinases"[Mesh] OR "Janus Kinase Inhibitors"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR "janus tyrosine kinase"[Title/Abstract] OR "protein tyrosine kinase janus"[Title/Abstract] OR

tsDMARD\*[Title/Abstract] OR "targeted synthetic DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR  
 "tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR  
 "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR  
 "upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR  
 Rinvoq[Title/Abstract] OR "GLPG0634"[Supplementary Concept] OR "GLPG0634"[All Fields] OR  
 "filgotinib"[All Fields] OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[All Fields] OR  
 "apremilast"[Supplementary Concept] OR "apremilast"[All Fields]))  
 NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))  
 NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR  
 "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical  
 Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development  
 Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published  
 Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type])

#### Embase (Elsevier): 621 resultados

('Arthritis, Psoriatic'/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab)

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn) OR

('interleukin 23'/exp OR IL-23:ti,ab OR 'il 23':ti,ab OR 'interleukin 23':ti,ab OR 'interleukin-23':ti,ab OR 'risankizumab'/exp OR 'abbv 066':ti,ab,tn,dn OR 'abbv066':ti,ab,tn,dn OR 'bi 655066':ti,ab,tn,dn OR 'bi655066':ti,ab,tn,dn OR 'risankizumab':ti,ab,tn,dn OR 'risankizumab rzaa':ti,ab,tn,dn OR 'risankizumab-rzaa':ti,ab,tn,dn OR 'skyrizi':ti,ab,tn,dn OR 'guselkumab'/exp OR 'cnto 1959':ti,ab,kw OR 'cnto1959':ti,ab,kw OR 'guselkumab':ti,ab,kw OR 'tremfya':ti,ab,kw OR 'tildrakizumab'/exp OR 'ilumetri':ti,ab,tn,dn OR 'ilumya':ti,ab,tn,dn OR 'mk 3222':ti,ab,tn,dn

OR 'mk3222':ti,ab,tn,dn OR 'sch 900222':ti,ab,tn,dn OR 'sch900222':ti,ab,tn,dn OR 'sunpg 1622':ti,ab,tn,dn OR 'sunpg 1623':ti,ab,tn,dn OR 'sunpg1622':ti,ab,tn,dn OR 'sunpg1623':ti,ab,tn,dn OR 'tildrakizumab':ti,ab,tn,dn OR 'tildrakizumab asmn':ti,ab,tn,dn OR 'tildrakizumab-asmn':ti,ab,tn,dn)

OR ('janus kinase')/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti OR

'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp 690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550' OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib' OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR

'upadacitinib' /exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide tarrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide tarrate' OR 'abt 494' OR 'abt494' OR 'rinvoq' OR 'upadacitinib' OR 'upadacitinib 2, 3 dihydroxybutanedioate' OR 'upadacitinib hemihydrate' OR 'upadacitinib hydrate' OR 'upadacitinib tarrate' OR

'deucravacitinib'/exp OR '6 (cyclopropanecarbonylamino) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropanecarbonylamino) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n [ (2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl)



dioxo 2, 3 dihydro 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 1h isoindol 4 yl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'otezla':ti,ab,kw))

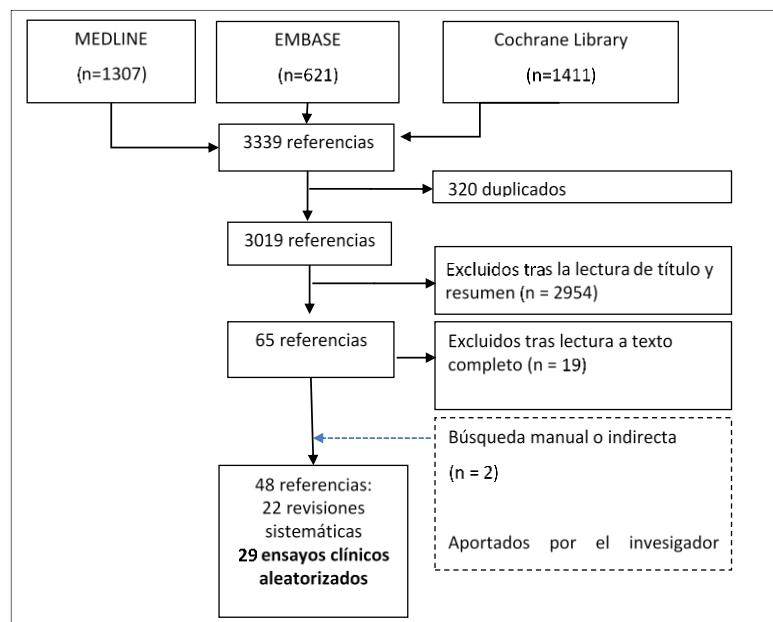
AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp OR 'cross sectional studies'/exp OR 'observational study'/exp  
OR 'case control studies'/exp OR 'case report'/exp)

### Cochrane Library: 1411 resultados

#### ID      Search Hits

|     |  |       |
|-----|--|-------|
| #1  | MeSH descriptor: [Arthritis, Psoriatic] explode all trees  | 542   |
| #2  | ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath*" OR "Arthropathy psoria*" OR "arthritis psoriatica" OR "Psoriatic rheumatism" OR "arthritis psoriatica"):ti,ab,kw  | 2738  |
| #3  | (arthritis NEAR/3 "Psoria*"):ti,ab,kw OR (Psoria* NEAR/3 arthritis):ti,ab,kw   | 2826  |
| #4  | #1 OR #2 OR #3   | 2829  |
| #5  | MeSH descriptor: [Interleukin-17] explode all trees  | 223   |
| #6  | MeSH descriptor: [Receptors, Interleukin-17] explode all trees   | 17    |
| #7  | ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR "secukinumab" OR 'cosentyx' OR "brodalumab" OR "bimekizumab"):ti,ab,kw  | 3882  |
| #8  | #5 OR #6 OR #7   | 3882  |
| #9  | MeSH descriptor: [Interleukin-23] explode all trees  | 109   |
| #10 | ("interleukin-23" OR "Interleukin 23" OR "IL-23" OR "IL 23" OR "risankizumab" OR "guselkumab" OR "tildrakizumab")  | 6059  |
| #11 | #9 OR #10  | 6073  |
| #12 | MeSH descriptor: [Janus Kinases] explode all trees   | 160   |
| #13 | MeSH descriptor: [Janus Kinase Inhibitors] explode all trees   | 105   |
| #14 | ("janus kinase*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD* OR "targeted synthetic DMARD*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR "GLPG0634" OR "filgotinib" OR deucravacitinib OR apremilast):ti,ab,kw | 4554  |
| #15 | #12 OR #13 OR #14  | 4560  |
| #16 | #8 OR #11 OR #15   | 12839 |
| #17 | #4 AND #16   | 1411  |

### Diagrama de flujo de los artículos



## Treatment with biologic or targeted synthetic disease-modifying antirheumatic drugs compared to TNF inhibitors

### Clinical question

In PsA, what is the efficacy, effectiveness and safety of IL-17, IL-23 and JAK inhibitors compared to TNF inhibitors?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

### Medline (Pubmed): 657 resultados

("Arthritis, Psoriatic"[Mesh] OR "Arthritis Psoriatic"[Title/Abstract] OR "Arthritic Psoriasis"[Title/Abstract] OR "psoriatic arthritis"[Title/Abstract] OR "psoriasis arthritis"[Title/Abstract] OR "psoriatic arthropath\*"[Title/Abstract] OR "Arthropathy psoria\*"[Title/Abstract] OR "arthritis psoriatica"[Title/Abstract] OR "Psoriatic rheumatism"[Title/Abstract])

AND

((("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17"[Title/Abstract] OR "IL 17"[Title/Abstract] OR "ixekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[Title/Abstract] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract]))

OR

("Interleukin-23"[Mesh] OR "interleukin-23"[Title/Abstract] OR "Interleukin 23"[Title/Abstract] OR "IL-23"[Title/Abstract] OR "IL 23"[Title/Abstract] OR "risankizumab"[Supplementary Concept] OR "risankizumab"[Title/Abstract] OR "guselkumab"[Supplementary Concept] OR "guselkumab"[Title/Abstract] OR "tildrakizumab"[Supplementary Concept] OR "tildrakizumab"[Title/Abstract]) OR ("APY0201" [Supplementary Concept] OR "Interleukin 12-23"[Title/Abstract] OR "IL-12-23"[Title/Abstract] OR "interleukin-12-23"[Title/Abstract] OR "IL-12-23 inhibitor\*"[Title/Abstract] OR "IL 12-23"[Title/Abstract] OR "IL 12,23"[Title/Abstract] OR "IL 12/23"[Title/Abstract] OR "Ustekinumab"[Mesh] OR "Ustekinumab"[Title/Abstract] OR Stelara[Title/Abstract])

OR ("Janus Kinases"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR

tsDMARD\*[Title/Abstract] OR "targeted synthetic DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR

"tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR  
 "upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR Rinvoq[Title/Abstract]  
 OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[All Fields]))  
 AND ("Receptors, Tumor Necrosis Factor"[Mesh] OR "Antibodies, Monoclonal"[Mesh] OR "Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh] OR "tumor necrosis factor-alpha antagonists"[Title/Abstract] OR "tumor necrosis factor-alpha inhibitor\*"[Title/Abstract] OR "anti-tumor necrosis factor-alpha"[Title/Abstract] OR "anti-tumor necrosis factor agent"[All Fields] OR "anti-tnf alpha"[Title/Abstract] OR "anti-TNF"[Title/Abstract] OR "anti-tumor necrosis factor alpha"[Title/Abstract] OR "anti TNF alpha"[Title/Abstract] OR "TNF alpha inhibitor\*"[Title/Abstract])  
 OR "infliximab"[Mesh] OR infliximab[Title/Abstract] OR remicade[Title/Abstract] OR avakine[All Fields] OR  
 "Etanercept"[Mesh] OR etanercept[All Fields] OR enbrel[All Fields] OR tunex[All Fields] OR  
 "adalimumab"[Mesh] OR adalimumab[Title/Abstract] OR humira[All Fields] OR  
 "certolizumab pegol"[Mesh] OR certolizumab[All Fields] OR cimzia[Title/Abstract] OR  
 "golimumab"[Supplementary Concept] OR golimumab[All Fields] OR simponi[All Fields])  
 NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))  
 NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type]))

### Embase (Elsevier): 576 resultados

('Arthritis, Psoriatic'/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab)

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn

OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn) OR

('interleukin 23'/exp OR IL-23:ti,ab OR 'il 23':ti,ab OR 'interleukin 23':ti,ab OR 'interleukin-23':ti,ab OR 'risankizumab'/exp OR 'abbv 066':ti,ab,tn,dn OR 'abbv066':ti,ab,tn,dn OR 'bi 655066':ti,ab,tn,dn OR 'bi655066':ti,ab,tn,dn OR 'risankizumab':ti,ab,tn,dn OR 'risankizumab rzaa':ti,ab,tn,dn OR 'risankizumab-rzaa':ti,ab,tn,dn OR 'skyrizi':ti,ab,tn,dn OR 'guselkumab'/exp OR 'cnto 1959':ti,ab,kw OR 'cnto1959':ti,ab,kw OR 'guselkumab':ti,ab,kw OR 'tremfya':ti,ab,kw OR 'tildrakizumab'/exp OR 'ilumetri':ti,ab,tn,dn OR 'ilumya':ti,ab,tn,dn OR 'mk 3222':ti,ab,tn,dn OR 'mk3222':ti,ab,tn,dn OR 'sch 900222':ti,ab,tn,dn OR 'sch900222':ti,ab,tn,dn OR 'sunpg 1622':ti,ab,tn,dn OR 'sunpg 1623':ti,ab,tn,dn OR 'sunpg1622':ti,ab,tn,dn OR 'sunpg1623':ti,ab,tn,dn OR 'tildrakizumab':ti,ab,tn,dn OR 'tildrakizumab asmn':ti,ab,tn,dn OR 'tildrakizumab-asmn':ti,ab,tn,dn)

OR ('Interleukin 12-23':ti,ab OR IL-12-23:ti,ab OR interleukin-12-23:ti,ab OR 'IL-12-23 inhibitor\*':ti,ab OR 'IL 12-23':ti,ab OR 'IL 12,23':ti,ab OR 'IL 12/23':ti,ab OR 'ustekinumab'/exp OR 'abp 654':ti,ab,tn,dn OR 'abp654':ti,ab,tn,dn OR 'avt 04':ti,ab,tn,dn OR 'avt04':ti,ab,tn,dn OR 'cnto 1275':ti,ab,tn,dn OR 'cnto1275':ti,ab,tn,dn OR 'ct p43':ti,ab,tn,dn OR 'ctp43':ti,ab,tn,dn OR 'fyb 202':ti,ab,tn,dn OR 'fyb202':ti,ab,tn,dn OR 'monoclonal antibody cnto 1275':ti,ab,tn,dn OR 'sb 17':ti,ab,tn,dn OR 'sb17':ti,ab,tn,dn OR 'stelara':ti,ab,tn,dn OR 'ustekinumab':ti,ab,tn,dn)

OR ('janus kinase'/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti OR

'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp 690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550' OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib' OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR

'upadacitinib'/exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide tartrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidine carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidine carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidine carboxamide'

AND

('tumor necrosis factor receptor')/exp OR 'tumor necrosis factor'/exp OR 'monoclonal antibody'/exp OR 'tnf alfa' OR 'tnf alpha' OR 'human recombinant tumour necrosis factor alpha' OR 'tissue necrosis factor' OR 'tumor necrosis factor' OR 'tumor necrosis factor alfa' OR 'tumor necrosis factor alpha' OR 'tumor necrosis factor-alpha' OR 'tumor necrosis factors' OR 'tumor necrosis serum' OR 'tumour necrosis factor' OR 'tumour necrosis factor alfa' OR 'tumour necrosis factor alpha' OR 'tumour necrosis factor-alpha' OR 'tumour necrosis factors' OR 'tumour necrosis serum' OR 'anti-tumor necrosis factor agent':ab,ti OR 'tumor necrosis

factor-alpha antagonists':ti,ab OR 'tumor necrosis factor-alpha inhibitor\*':ti,ab OR "anti-tumor necrosis factor-alpha":ab,ti OR "anti-TNF":ab,ti OR "anti-tumor necrosis factor alpha":ab,ti OR "anti TNF":ab,ti OR 'anti TNF alpha':ti,ab OR "TNF alpha inhibitor\*":ab,ti OR 'infliximab':exp OR infliximab:ab,ti OR remicade:ab,ti OR avakine:ab,ti OR 'etanercept':exp OR etanercept:ab,ti OR enbrel:ab,ti OR tunex:ab,ti OR 'adalimumab':exp OR adalimumab:ab,ti OR humira:ab,ti OR 'certolizumab pegol':exp OR 'cdp 870':ab,ti OR 'cdp870':ab,ti OR 'certolizumab':ab,ti OR 'cimzia':ab,ti OR 'golimumab':exp OR 'cnto 148':ab,ti OR 'cnto148':ab,ti OR 'golimumab':ab,ti OR 'simponi':ab,ti)

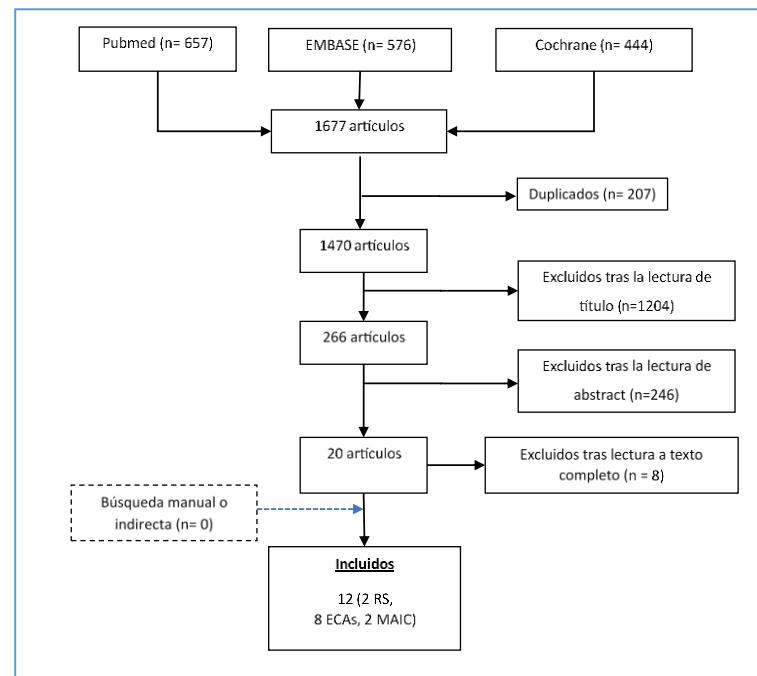
AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp OR 'cross sectional studies'/exp OR 'observational study'/exp  
OR 'case control studies'/exp OR 'case report'/exp)

### Cochrane Library: 444 resultados

| ID  | Search Hits   |
|-----|---|
| #1  | MeSH descriptor: [Arthritis, Psoriatic] explode all trees 540   |
| #2  | ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath*" OR "Arthropathy psoria*" OR "arthritis psoriatica" OR "Psoriatic rheumatism"):ti,ab,kw 2729  |
| #3  | (arthritis NEAR/3 "Psoriasis" ) OR (Psoria* NEAR/3 arthritis) 2948  |
| #4  | #1 OR #2 OR #3 2951   |
| #5  | MeSH descriptor: [Interleukin-17] explode all trees 223   |
| #6  | MeSH descriptor: [Receptors, Interleukin-17] explode all trees 17   |
| #7  | ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR "secukinumab" OR 'cosentyx' OR "brodalumab" OR "bimekizumab"):ti,ab,kw 3871  |
| #8  | MeSH descriptor: [Ustekinumab] explode all trees 243  |
| #9  | ("Interleukin 12-23" OR "Interleukin 12/23" OR "IL-12-23" OR "interleukin-12-23" OR "IL-12-23 inhibitor*" OR "IL 12-23" OR "IL 12,23" OR "IL 12/23" OR Ustekinumab OR Stelara):ti,ab,kw 1123  |
| #10 | #5 OR #6 OR #7 OR #8 OR #9 4758   |
| #11 | MeSH descriptor: [Interleukin-23] explode all trees 108   |
| #12 | ("interleukin-23" OR "Interleukin 23" OR "IL-23" OR "IL 23" OR "risankizumab" OR "guselkumab" OR "tildrakizumab") 6046  |
| #13 | #11 OR #12 6060   |
| #14 | MeSH descriptor: [Janus Kinases] explode all trees 160  |
| #15 | MeSH descriptor: [Janus Kinase Inhibitors] explode all trees 105  |
| #16 | ("janus kinase*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD* OR "targeted synthetic DMARD*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR deucravacitinib):ti,ab,kw 3885 |
| #17 | #14 OR #15 OR #16 3891  |
| #18 | #10 OR #13 OR #17 12858   |
| #19 | #4 AND #18 1381   |
| #20 | MeSH descriptor: [Receptors, Tumor Necrosis Factor] explode all trees 1366  |
| #21 | MeSH descriptor: [Antibodies, Monoclonal] explode all trees 16064   |
| #22 | MeSH descriptor: [Tumor Necrosis Factor-alpha] explode all trees 3332   |

- #23 ("tumor necrosis factor-alpha antagonists" OR "tumor necrosis factor-alpha inhibitor\*" OR "anti-tumor necrosis factor-alpha" OR "anti-tnf alpha" OR "anti-TNF" OR "anti-tumor necrosis factor alpha" OR "anti TNF alpha" OR "TNF alpha inhibitor\*"):ab,ti,kw 997
- #24 MeSH descriptor: [Infliximab] explode all trees 802
- #25 MeSH descriptor: [Etanercept] explode all trees 811
- #26 MeSH descriptor: [Adalimumab] explode all trees 882
- #27 MeSH descriptor: [Certolizumab Pegol] explode all trees 187
- #28 (infliximab OR remicade OR avakine OR etanercept OR enbrel OR tunex OR adalimumab OR humira OR certolizumab OR cimzia OR golimumab OR simponi):ti,ab,kw 8432
- #29 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 25688
- #30 #19 AND #29 444

#### Diagrama de flujo de los artículos



## Extra-musculoskeletal manifestations

### Clinical question

In PsA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)?

**En cuanto al diseño de estudios se han considerado para su inclusión: metanálisis o revisiones sistemáticas de ECA, ECA.**

### Medline (Pubmed): 2893 resultados

("Arthritis, Psoriatic"[Mesh] OR "Arthritis Psoriatic"[Title/Abstract] OR "Arthritic Psoriasis"[Title/Abstract] OR "psoriatic arthritis"[Title/Abstract] OR "psoriasis arthritis"[Title/Abstract] OR "psoriatic arthropath\*"[Title/Abstract] OR "Arthropathy psoria\*"[Title/Abstract] OR "arthritis psoriatica"[Title/Abstract] OR "Psoriatic rheumatism"[Title/Abstract])

AND

(("Interleukin-17"[Mesh] OR "Receptors, Interleukin-17"[Mesh] OR "Interleukin 17"[Title/Abstract] OR IL-17[Title/Abstract] OR interleukin-17[Title/Abstract] OR "IL-17 inhibitor\*"[Title/Abstract] OR "IL-17 blocker\*"[Title/Abstract] OR "IL-17"[Title/Abstract] OR "IL 17"[Title/Abstract] OR "ixekizumab"[Supplementary Concept] OR "ixekizumab"[Title/Abstract] OR taltz[Title/Abstract] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[Title/Abstract] OR cosentyx[Title/Abstract] OR "brodalumab"[Supplementary Concept] OR "brodalumab"[Title/Abstract] OR lumicef[Title/Abstract] OR siliq[Title/Abstract] OR "kyntheum"[Title/Abstract] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[Title/Abstract] OR bimzel\*[Title/Abstract]))

OR

("Interleukin-23"[Mesh] OR "interleukin-23"[Title/Abstract] OR "Interleukin 23"[Title/Abstract] OR "IL-23"[Title/Abstract] OR "IL 23"[Title/Abstract] OR "risankizumab"[Supplementary Concept] OR "risankizumab"[Title/Abstract] OR skyrizi[Title/Abstract] OR "guselkumab"[Supplementary Concept] OR "guselkumab"[Title/Abstract] OR tremfya[Title/Abstract] OR "tildrakizumab"[Supplementary Concept] OR "tildrakizumab"[Title/Abstract] OR ilumetri[Title/Abstract] OR ilumya[Title/Abstract]))

OR ("APY0201" [Supplementary Concept] OR "Interleukin 12-23"[Title/Abstract] OR "IL-12-23"[Title/Abstract] OR "interleukin-12-23"[Title/Abstract] OR "IL 12-23" [Title/Abstract] OR "IL 12,23"[Title/Abstract] OR "IL 12/23"[Title/Abstract] OR "Ustekinumab"[Mesh] OR "Ustekinumab"[Title/Abstract] OR Stelara[Title/Abstract] OR Abatacept)

OR ("Janus Kinases"[Mesh] OR "Janus Kinase Inhibitors"[Mesh] OR "janus kinase"[Title/Abstract] OR JAK[Title/Abstract] OR "jakinibs"[Title/Abstract] OR "janus associated kinase\*"[Title/Abstract] OR Jakavi[Title/Abstract] OR "janus tyrosine kinase"[Title/Abstract] OR "protein tyrosine kinase janus"[Title/Abstract] OR

tsDMARD\*[Title/Abstract] OR "targeted synthetic DMARDs"[Title/Abstract] OR "targeted synthetic DMARD"[Title/Abstract] OR  
 "tofacitinib"[Supplementary Concept] OR "tofacitinib"[Title/Abstract] OR  
 "tasocitinib"[Title/Abstract] OR "Xeljanz"[Title/Abstract] OR  
 "upadacitinib"[Supplementary Concept] OR "upadacitinib"[Title/Abstract] OR  
 Rinvoq[Title/Abstract] OR "GLPG0634"[Supplementary Concept] OR "GLPG0634"[All Fields] OR  
 "filgotinib"[All Fields] OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[All Fields] OR  
 "apremilast"[Supplementary Concept] OR "apremilast"[All Fields])  
 OR  
 ("Receptors, Tumor Necrosis Factor"[Mesh] OR "Antibodies, Monoclonal"[Mesh] OR "Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh] OR "tumor necrosis factor-alpha antagonists"[Title/Abstract] OR "tumor necrosis factor-alpha inhibitor\*"[Title/Abstract] OR "anti-tumor necrosis factor-alpha"[Title/Abstract] OR "anti-tumor necrosis factor agent"[All Fields] OR "anti-tnf alpha"[Title/Abstract] OR "anti-TNF"[Title/Abstract] OR "anti-tumor necrosis factor alpha"[Title/Abstract] OR "anti TNF alpha"[Title/Abstract] OR "TNF alpha inhibitor\*"[Title/Abstract])  
 OR "infliximab"[Mesh] OR infliximab[Title/Abstract] OR remicade[Title/Abstract] OR  
 avakine[All Fields] OR  
 "Etanercept"[Mesh] OR etanercept[All Fields] OR enbrel[All Fields] OR tunex[All Fields] OR  
 "adalimumab"[Mesh] OR adalimumab[Title/Abstract] OR humira[All Fields] OR  
 "certolizumab pegol"[Mesh] OR certolizumab[All Fields] OR cimzia[Title/Abstract] OR  
 "golimumab"[Supplementary Concept] OR golimumab[All Fields] OR simponi[All Fields]))

AND

("uveitis"[MeSH Terms] OR "uveitis"[All Fields] OR "uveitides"[All Fields] OR uveitis OR psoria\* OR "inflammatory bowel diseases"[MeSH Terms] OR "inflammatory bowel diseases"[All Fields] OR "inflammatory bowel disease"[All Fields] OR "IBD"[All Fields] OR "crohn"[All Fields] OR "crohn s"[All Fields] OR "crohn's"[All Fields] OR "crohns"[All Fields] OR "colitis, ulcerative"[MeSH Terms] OR "ulcerative colitis"[All Fields])

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))

NOT ("cross sectional studies"[MeSH Terms] OR "observational study"[Publication Type] OR "case reports"[Publication Type] OR "case control studies"[MeSH Terms] OR "Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type])

### Embase (Elsevier): 621 resultados

('Arthritis, Psoriatic'/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic

arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab)

AND

(('interleukin 17'/exp OR 'ctla 8':ti,ab OR 'ctla8':ti,ab OR 'il-17':ti,ab OR 'cytotoxic t lymphocyte antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated antigen 8':ti,ab OR 'cytotoxic t lymphocyte associated protein 8':ti,ab OR 'cytotoxic t lymphocyte protein 8':ti,ab OR 'il 17a':ti,ab OR 'interleukin 17':ti,ab OR 'interleukin 17a':ti,ab OR 'interleukin-17':ti,ab OR 'ixekizumab'/exp OR 'ixekizumab':ti,ab,tn,dn OR 'ly 2439821':ti,ab,tn,dn OR 'ly2439821':ti,ab,tn,dn OR 'taltz':ti,ab,tn,dn OR 'secukinumab'/exp OR 'ain 457':ti,ab,tn,dn OR 'ain457':ti,ab,tn,dn OR 'bat 2306':ti,ab,tn,dn OR 'bat2306':ti,ab,tn,dn OR 'cosentyx':ti,ab,tn,dn OR 'kb 03303a':ti,ab,tn,dn OR 'kb03303a':ti,ab,tn,dn OR 'scapho':ti,ab,tn,dn OR 'secukinumab':ti,ab,tn,dn OR 'ts 1808':ti,ab,tn,dn OR 'ts1808':ti,ab,tn,dn OR 'brodalumab'/exp OR 'amg 827':ti,ab,tn,dn OR 'amg827':ti,ab,tn,dn OR 'brodalumab':ti,ab,tn,dn OR 'khk 4827':ti,ab,tn,dn OR 'khk4827':ti,ab,tn,dn OR 'kyntheum':ti,ab,tn,dn OR 'lumicef':ti,ab,tn,dn OR 'siliq':ti,ab,tn,dn OR 'bimekizumab'/exp OR 'bimekizumab':ti,ab,tn,dn OR 'bimzelx':ti,ab,tn,dn OR 'cdp 4940':ti,ab,tn,dn OR 'cdp4940':ti,ab,tn,dn OR 'ucb 4940':ti,ab,tn,dn OR 'ucb4940':ti,ab,tn,dn) OR

('interleukin 23'/exp OR IL-23:ti,ab OR 'il 23':ti,ab OR 'interleukin 23':ti,ab OR 'interleukin-23':ti,ab OR 'risankizumab'/exp OR 'abbv 066':ti,ab,tn,dn OR 'abbv066':ti,ab,tn,dn OR 'bi 655066':ti,ab,tn,dn OR 'bi655066':ti,ab,tn,dn OR 'risankizumab':ti,ab,tn,dn OR 'risankizumab rzaa':ti,ab,tn,dn OR 'risankizumab-rzaa':ti,ab,tn,dn OR 'skyrizi':ti,ab,tn,dn OR 'guselkumab'/exp OR 'cnto 1959':ti,ab,kw OR 'cnto1959':ti,ab,kw OR 'guselkumab':ti,ab,kw OR 'tremfya':ti,ab,kw OR 'tildrakizumab'/exp OR 'ilumetri':ti,ab,tn,dn OR 'ilumya':ti,ab,tn,dn OR 'mk 3222':ti,ab,tn,dn OR 'mk3222':ti,ab,tn,dn OR 'sch 900222':ti,ab,tn,dn OR 'sch900222':ti,ab,tn,dn OR 'sunpg 1622':ti,ab,tn,dn OR 'sunpg1622':ti,ab,tn,dn OR 'sunpg 1623':ti,ab,tn,dn OR 'sunpg1623':ti,ab,tn,dn OR 'tildrakizumab':ti,ab,tn,dn OR 'tildrakizumab asmn':ti,ab,tn,dn OR 'tildrakizumab-asmn':ti,ab,tn,dn)

OR ('janus kinase'/exp OR 'jak protein' OR 'janus kinase':ti,ab OR 'janus kinases' OR 'janus tyrosine kinase' OR 'protein jak' OR 'protein tyrosine kinase janus' OR 'protein tyrosine kinase janus kinase' OR 'tyrosine kinase janus kinase' OR "janus associated kinase":ab,ti OR Jakavi:ab,ti OR JAK:ab,ti OR "jakinibs":ab,ti OR tsDMARD\*:ab,ti OR "targeted synthetic DMARDs":ab,ti OR "targeted synthetic DMARD":ab,ti OR

'tofacitinib'/exp OR '1 cyanoacetyl 4 methyl n methyl n (1h pyrrolo [2, 3 d] pyrimidin 4 yl) 3 piperidinamine' OR '3 [4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] 1 piperidinyl] 3 oxopropanenitrile' OR '4 [n [1 (2 cyano 1 oxoethyl) 4 methyl 3 piperidinyl] n methylamino] pyrrolo [2, 3 d] pyrimidine' OR '4 methyl 3 [methyl (7h pyrrolo [2, 3 d] pyrimidin 4 yl) amino] beta oxo 1 piperidinepropanenitrile' OR 'cp 690 550' OR 'cp 690, 550' OR 'cp 690550' OR 'cp 690550 10' OR 'cp 690550-10' OR 'cp690 550' OR 'cp690, 550' OR 'cp690550' OR 'cp690550 10' OR 'cp690550-10' OR 'tasocitinib':ab,ti OR 'tasocitinib citrate' OR 'tofacitinib' OR 'tofacitinib citrate' OR 'xeljanz':ab,ti OR 'xeljanz xr' OR

'upadacitinib'/exp OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1 pyrrolidinecarboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) 1

pyrrolidinecarboxamide tartrate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide 2, 3 dihydroxybutanedioate' OR '3 ethyl 4 (3h imidazo [1, 2 a] pyrrolo [2, 3 e] pyrazin 8 yl) n (2, 2, 2 trifluoroethyl) pyrrolidine 1 carboxamide tartrate' OR 'abt 494' OR 'abt494' OR 'rinvog' OR 'upadacitinib' OR 'upadacitinib 2, 3 dihydroxybutanedioate' OR 'upadacitinib hemihydrate' OR 'upadacitinib hydrate' OR 'upadacitinib tartrate' OR 'deucravacitinib'/exp OR '6 (cyclopropanecarbonylamino) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropanecarbonylamino) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) phenyl] amino] n (trideuteriomethyl) pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1, 2, 4 triazol 3 yl) anilino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 (cyclopropylcarboxamide) 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) 3 pyridazinecarboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) phenyl] amino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [ [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl d3) 3 pyridazinecarboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n [(2h3) methyl] pyridazine 3 carboxamide':ti,ab,tn,dn OR '6 [ (cyclopropylcarbonyl) amino] 4 [2 methoxy 3 (1 methyl 1h 1, 2, 4 triazol 3 yl) anilino] n (methyl) pyridazine 3 carboxamide h 3':ti,ab,tn,dn OR 'bms 986165':ti,ab,tn,dn OR 'bms 986165 01':ti,ab,tn,dn OR 'bms 98616501':ti,ab,tn,dn OR 'bms 98616501':ti,ab,tn,dn OR 'bms986165':ti,ab,tn,dn OR 'bms986165':ti,ab,tn,dn OR 'bms98616501':ti,ab,tn,dn OR 'deucravacitinib':ti,ab,tn,dn OR 'tyk2-in-4':ti,ab,tn,dn OR 'filgotinib':exp OR 'filgotinib':ti,ab,tn,dn OR 'filgotinib 2 butenedioate':ti,ab,tn,dn OR 'filgotinib hydrochloride':ti,ab,tn,dn OR 'filgotinib maleate':ti,ab,tn,dn OR 'g 146034':ti,ab,tn,dn OR 'g 146034 101':ti,ab,tn,dn OR 'g 146034-101':ti,ab,tn,dn OR 'g146034':ti,ab,tn,dn OR 'g146034 101':ti,ab,tn,dn OR 'g146034-101':ti,ab,tn,dn OR 'glpg 0634':ti,ab,tn,dn OR

'glpg0634':ti,ab,tn,dn OR 'gs 6034':ti,ab,tn,dn OR 'gs6034':ti,ab,tn,dn OR 'jyseleca':ti,ab,tn,dn  
OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl]  
cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1,  
2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2 butenedioate':ti,ab,tn,dn OR 'n [5  
[4 (1, 1 dioxothiomorpholinomethyl) phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl]  
cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4  
thiomorpholinyl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl]  
cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxido 4 thiomorpholinyl) methyl]  
phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide 2  
butenedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxothiomorpholin 4 yl) methyl] phenyl] 1, 2, 4  
triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn OR 'n [5 [4 [(1, 1  
dioxothiomorpholin 4 yl) methyl] phenyl] 1, 2, 4 triazolo [1, 5 a] pyridin 2 yl]  
cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn OR 'n [5 [4 [(1, 1 dioxothiomorpholin 4  
yl) methyl] phenyl] [1, 2, 4] triazolo [1, 5 a] pyridin 2 yl] cyclopropanecarboxamide':ti,ab,tn,dn  
OR 'n [5 [4 [(1, 1 dioxothiomorpholin 4 yl) methyl] phenyl] [1, 2, 4] triazolo [1, 5 a] pyridin 2 yl]  
cyclopropanecarboxamide but 2 enedioate':ti,ab,tn,dn)

OR ('apremilast'/exp OR 'ap 506':ti,ab,kw OR 'ap506':ti,ab,kw OR 'apremilast':ti,ab,kw OR 'cc 10004':ti,ab,kw OR 'cc10004':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methanesulfonyl) ethyl] 1, 3 dioxo 2, 3 dihydro 1h isoindol 4 yl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methanesulfonyl) ethyl] 1, 3 dioxo 2, 3 dihydro 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methanesulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 1h isoindol 4 yl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methanesulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 1, 3 dioxo 2, 3 dihydro 1h isoindol 4 yl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 1, 3 dioxo 2, 3 dihydro 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 1h isoindol 4 yl] acetamide':ti,ab,kw OR 'n [2 [1 (3 ethoxy 4 methoxyphenyl) 2 (methylsulfonyl) ethyl] 2, 3 dihydro 1, 3 dioxo 4 (1h) isoindolyl] acetamide':ti,ab,kw OR 'otezla':ti,ab,kw))

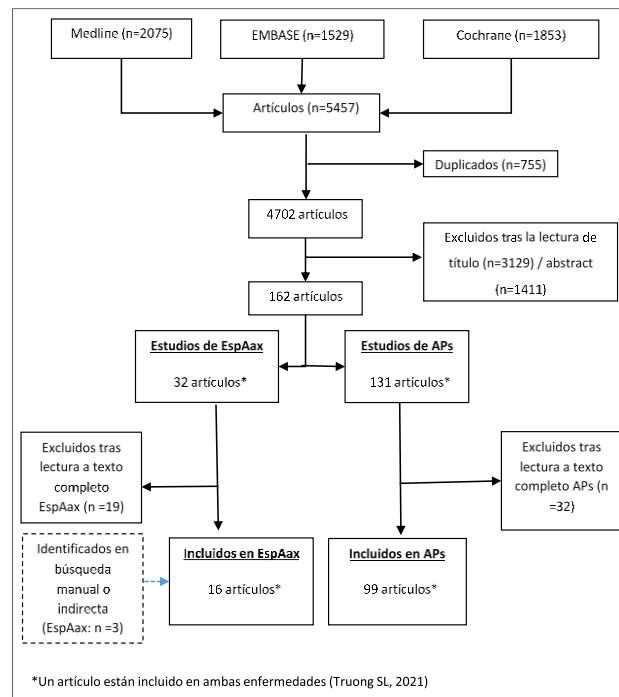
AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp OR 'cross sectional studies'/exp OR 'observational study'/exp  
OR 'case control studies'/exp OR 'case report'/exp)

Cochrane Library: 1411 resultados

| ID | Search Hits  |
|----|--|
| #1 | MeSH descriptor: [Arthritis, Psoriatic] explode all trees 542  |
| #2 | ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath*" OR "Arthropathy psoria*" OR "arthritis psoriatica" OR "Psoriatic rheumatism" OR "arthritis psoriatica"):ti,ab,kw 2738 |
| #3 | (arthritis NEAR/3 "Psoria*") :ti,ab,kw OR (Psoria* NEAR/3 arthritis) :ti,ab,kw 2826  |
| #4 | #1 OR #2 OR #3 2829  |
| #5 | MeSH descriptor: [Interleukin-17] explode all trees 223  |
| #6 | MeSH descriptor: [Receptors, Interleukin-17] explode all trees 17  |

- #7 ("interleukin 17" OR IL-17 OR interleukin-17 OR "IL 17" OR "ixekizumab" OR "secukinumab" OR 'cosentyx' OR "brodalumab" OR "bimekizumab"):ti,ab,kw 3882
- #8 #5 OR #6 OR #7 3882
- #9 MeSH descriptor: [Interleukin-23] explode all trees 109
- #10 ("interleukin-23" OR "Interleukin 23" OR "IL-23" OR "IL 23" OR "risankizumab" OR "guselkumab" OR "tildrakizumab") 6059
- #11 #9 OR #10 6073
- #12 MeSH descriptor: [Janus Kinases] explode all trees 160
- #13 MeSH descriptor: [Janus Kinase Inhibitors] explode all trees 105
- #14 ("janus kinase\*" OR JAK OR jakinibs OR Jakavi OR "janus associated kinase\*" OR Jakavi OR "janus tyrosine kinase" OR "protein tyrosine kinase janus" OR tsDMARD\* OR "targeted synthetic DMARD\*" OR "targeted synthetic DMARD" OR Tofacitinib OR "tasocitinib" OR "Xeljanz" OR upadacitinib OR Rinvoq OR "GLPG0634" OR "filgotinib" OR deucravacitinib OR apremilast):ti,ab,kw 4554
- #15 #12 OR #13 OR #14 4560
- #16 #8 OR #11 OR #15 12839
- #17 #4 AND #16 1411

### Diagrama de flujo de los artículos



## Obesity and smoking

### Clinical question

In PsA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

**En cuanto al diseño de estudios se han considerado para su inclusión: subanálisis de ensayos clínicos, cohortes de expuestos vs. no expuestos, casos y controles.**

### Medline (Pubmed): 1397 resultados

(("Arthritis, Psoriatic"[Mesh] OR "Arthritis Psoriatic"[Title/Abstract] OR "Arthritic Psoriasis"[Title/Abstract] OR "psoriatic arthritis"[Title/Abstract] OR "psoriasis arthritis"[Title/Abstract] OR "psoriatic arthropath\*[Title/Abstract] OR "Arthropathy psoria\*[Title/Abstract] OR "arthritis psoriatica"[Title/Abstract] OR "Psoriatic rheumatism"[Title/Abstract]) OR ("Axial Spondyloarthritis"[Mesh] OR "Spondylitis, Ankylosing"[Mesh] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "axSpA"[Title/Abstract] OR "axial SpA"[Title/Abstract:~2] OR "Ankylosing Spondylitis"[Title/Abstract:~2] OR "axial spondyloarthritis"[Title/Abstract:~2] OR "non-radiographic axial spondyloarthritis"[Title/Abstract:~2] OR "nr-axSpA"[All Fields] OR "axial Ankylosing"[Title/Abstract:~2] OR "Spondylitis Ankylosing"[Title/Abstract:~2] OR "Spondylitis rheumatic"[Title/Abstract:~2] OR "Ankylosing Spondylarthritides"[Title/Abstract:~2]))

AND

(("cigarett\*"[All Fields] OR "cigar\*"[Title/Abstract] OR "snuff"[Title/Abstract] OR "tobacco products"[MeSH Terms] OR "Tobacco Use Disorder"[Mesh] OR "Tobacco Use"[Mesh] OR "tobacco product\*"[All Fields] OR "tobacco"[MeSH Terms] OR "tobacc\*"[Title/Abstract] OR "Smoke"[Mesh] OR "Smokers"[Mesh] OR "smok\*"[Title/Abstract] OR "smoking"[MeSH Terms] OR "Smoke Exposure"[Title/Abstract] OR Vaper[Title/Abstract] OR "Tobacco Use Cessation"[Mesh] OR "nicotine"[Title/Abstract]))

OR

("overweight"[MeSH Terms] OR "overweight\*"[All Fields] OR "body mass"[Title/Abstract] OR "body weight"[Title/Abstract] OR "body mass index"[Title/Abstract] OR BMI[Title/Abstract] OR "body mass index"[MeSH Terms] OR "body Weight"[Title/Abstract] OR "obesity"[MeSH Terms] OR "obese\*"[All Fields] OR "obesit\*"[All Fields]))

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))

NOT ("Clinical Conference"[Publication Type] OR "Congress"[Publication Type] OR "Consensus Development Conference"[Publication Type] OR "Editorial"[Publication Type] OR "Published Erratum"[Publication Type] OR "Letter"[Publication Type] OR "Comment"[Publication Type]))

### Embase (Elsevier): 2277 resultados

(('Arthritis, Psoriatic'/exp OR 'psoriatic arthritis'/exp OR 'arthritis psoriatic'/exp OR 'arthritis psoriatic':ab,ti OR 'Arthritic Psoriasis':ti,ab OR 'psoriatic arthritis':ti,ab OR 'psoriatic arthropathy'/exp OR 'psoriatic arthropathy':ab,ti OR 'psoriatic arthropath\*':ti,ab OR 'Arthropathy psoria\*':ti,ab OR 'psoriasis arthritis'/exp OR 'psoriasis arthritis':ti,ab OR 'arthritis psoriatica':ti,ab OR 'Psoriatic rheumatism':ti,ab) OR ('axial spondyloarthritis'/exp OR 'axspa (spondyloarthritis)':ti,ab OR 'axial spondylarthritis':ti,ab OR 'axial spondyloarthritis':ti,ab OR 'ankylosing spondylitis'/exp OR 'Spondylitis Ankylosing':ti,ab OR 'ankylosing spondylitis':ti,ab OR axSpA:ti,ab OR 'axial SpA':ti,ab OR 'axial spondyloarthritis':ab,ti OR 'non-radiographic axial spondyloarthritis':ti,ab OR nr-axSpA OR 'axial Ankylosing':ti,ab OR 'Spondylitis rheumatic':ab,ti OR 'Ankylosing Spondylarthritides':ti,ab OR (axial NEAR/3 spondyl\*) OR (axial NEAR/3 Ankylosing\*)))

AND

('cigarette smoking'/exp OR 'cigarette smoker':ti,ab,kw OR 'cigarette smoking':ti,ab,kw OR 'smoking, cigarette':ti,ab,kw OR 'cigarette'/exp OR 'cigarette\*':ti,ab,kw OR "cigar\*" OR 'filter cigarette':ti,ab,kw OR 'tobacco snuff'/exp OR 'snuff':ti,ab,kw OR 'snuff tobacco':ti,ab,kw OR 'tobacco snuff':ti,ab,kw OR 'tobacco use'/exp OR 'tobacco usage':ti,ab,kw OR 'tobacco use':ti,ab,kw OR "tobacco product\*":ti,ab,kw OR  
 'tobacco dependence'/exp OR 'dependence, tobacco':ti,ab,kw OR 'nicotine abuse':ti,ab,kw OR 'nicotine addiction':ti,ab,kw OR 'nicotine dependence':ti,ab,kw OR 'nicotine dependency':ti,ab,kw OR 'nicotinism':ti,ab,kw OR 'tobacco abuse':ti,ab,kw OR 'tobacco addiction':ti,ab,kw OR 'tobacco dependence':ti,ab,kw OR 'tobacco dependency':ti,ab,kw OR 'tobacco use disorder':ti,ab,kw OR 'tobaccoism':ti,ab,kw OR 'tobacco'/exp OR 'condensate, tobacco':ti,ab,kw OR 'tobacc\*':ti,ab,kw OR 'tobacco condensate':ti,ab,kw OR 'tobacco constituent':ti,ab,kw OR 'tobacco product':ti,ab,kw OR 'tobacco products':ti,ab,kw OR 'tobacco smoke condensate':ti,ab,kw OR 'tobacco smoke extract':ti,ab,kw OR 'tobacco smoke residue':ti,ab,kw OR 'smoke'/exp OR 'smok\*':ti,ab,kw OR 'smoking'/exp OR 'behavior, smoking':ti,ab,kw OR 'behaviour, smoking':ti,ab,kw OR 'reverse smoking':ti,ab,kw OR 'smoker':ti,ab,kw OR 'smokers':ti,ab,kw OR 'smoking':ti,ab,kw OR 'smoking behavior':ti,ab,kw OR 'smoking behaviour':ti,ab,kw OR 'tobacco smoking':ti,ab,kw OR 'smoke exposure':exp OR 'smoking cessation':exp OR 'abstination, smoking':ti,ab,kw OR 'abstinence from nicotine':ti,ab,kw OR 'abstinence from smoking':ti,ab,kw OR 'abstinence from tobacco':ti,ab,kw OR 'cessation, smoking':ti,ab,kw OR 'dehabituation, smoking':ti,ab,kw OR 'nicotine abstinence':ti,ab,kw OR 'nicotine abstinen':ti,ab,kw OR 'nicotine cessation':ti,ab,kw OR 'nicotine withdrawal':ti,ab,kw OR 'quit smoking':ti,ab,kw OR 'smoking abstinence':ti,ab,kw OR 'smoking cessation':ti,ab,kw OR 'smoking dehabituation':ti,ab,kw OR 'smoking, stopping':ti,ab,kw OR 'stop smoking':ti,ab,kw OR 'stopping smoking':ti,ab,kw OR 'tobacco use cessation':ti,ab,kw OR 'nicotine'/exp OR nicotine:ti,ab,kw OR Vaper:ti,ab,kw

OR

'body mass'/exp OR 'bmi':ti,ab,kw OR 'quetelet index':ti,ab,kw OR 'body ban mass':ti,ab,kw OR 'body mass':ti,ab,kw OR 'body mass index':ti,ab,kw OR 'body weight'/exp OR 'body weight':ti,ab,kw OR 'total body weight':ti,ab,kw OR 'weight, body':ti,ab,kw OR 'obesity'/exp OR 'adipose tissue hyperplasia':ti,ab,kw OR 'adipositas':ti,ab,kw OR 'adiposity':ti,ab,kw OR

'alimentary obesity':ti,ab,kw OR 'body weight, excess':ti,ab,kw OR 'corpulency':ti,ab,kw OR 'fat overload syndrome':ti,ab,kw OR 'nutritional obesity':ti,ab,kw OR 'obesitas':ti,ab,kw OR 'obesit\*':ti,ab,kw OR "obese\*":ti,ab,kw OR 'overweight\*':ti,ab,kw)

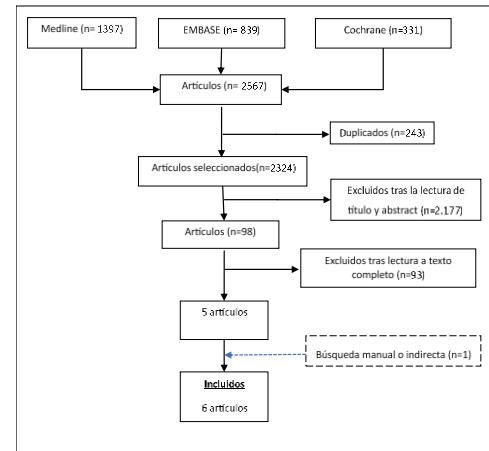
AND [embase]/lim NOT [medline]/lim NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))  
NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR  
[editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR  
'consensus development'/exp)

### Cochrane Library: 331 resultados

#### ID      Search Hits

|     |   |        |
|-----|---|--------|
| #1  | MeSH descriptor: [Axial Spondyloarthritis] explode all trees  | 835    |
| #2  | ("Spondylitis Ankylosing" OR "axial SpA" OR "axSpA" OR "Ankylosing Spondylitis" OR "axial spondyloarthritis" OR "axial Ankylosing" OR "non radiographic axial spondyloarthritis" OR nr-axSpA OR axspa OR "Spondylitis rheumatic" OR "Ankylosing Spondylarthritis"):ti,ab,kw | 2810   |
| #3  | (axial NEAR/3 spondyl*):ti,ab,kw OR (axial NEAR/3 Ankylosing*):ti,ab,kw   | 820    |
| #4  | MeSH descriptor: [Arthritis, Psoriatic] explode all trees   | 628    |
| #5  | ("psoriatic arthritis" OR "Arthritis Psoriatic" OR "Arthritic Psoriasis" OR "psoriasis arthritis" OR "psoriatic arthropath*" OR "Arthropathy psoria*" OR "arthritis psoriatica" OR "Psoriatic rheumatism" OR "arthritis psoriatica"):ti,ab,kw                               | 2809   |
| #6  | (arthritis NEAR/3 "Psoria*") :ti,ab,kw OR (Psoria* NEAR/3 arthritis):ti,ab,kw   | 2899   |
| #7  | #1 OR #2 OR #3 OR #4 OR #5 OR #6  | 5258   |
| #8  | MeSH descriptor: [Tobacco Products] explode all trees   | 646    |
| #9  | MeSH descriptor: [Tobacco Use Disorder] explode all trees   | 2016   |
| #10 | MeSH descriptor: [Tobacco Use] explode all trees  | 506    |
| #11 | MeSH descriptor: [Tobacco] explode all trees  | 286    |
| #12 | MeSH descriptor: [Tobacco Use Cessation] explode all trees  | 153    |
| #13 | MeSH descriptor: [Smoke] explode all trees  | 524    |
| #14 | MeSH descriptor: [Smokers] explode all trees  | 658    |
| #15 | MeSH descriptor: [Smoke] explode all trees  | 524    |
| #16 | MeSH descriptor: [Obesity] explode all trees  | 18204  |
| #17 | MeSH descriptor: [Overweight] explode all trees   | 21526  |
| #18 | MeSH descriptor: [Body Mass Index] explode all trees  | 12344  |
| #19 | ("cigaret**" OR "cigar*" OR "snuff" OR "tobacco product*" OR "tobacc*" OR "smok**" OR "Smoke Exposure" OR Vaper OR "nicotine"):ti,ab,kw   | 8739   |
| #20 | ("overweight*" OR "body mass" OR "body weight" OR BMI OR "obese*" OR "obesit*"):ti,ab,kw  | 140113 |
| #21 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20   | 152787 |
| #22 | #7 AND #21  | 331    |

### Diagrama de flujo de los artículos



## 4. GRADE Evidence tables to support the updated recommendations

### Treatment of Axial Spondyloarthritis

#### Biologic DMARD or JAK inhibitor therapy compared to placebo

##### Clinical question

In axSpA, what is the efficacy of IL-17 and JAK inhibitors compared to placebo?

#### Secukinumab vs placebo espondiloartritis axial

**Pregunta:** Secukinumab 150 mg y 300 mg/4 semanas comparado con placebo para espondiloartritis axial

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Secukinumab     | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

ASAS20 (seguimiento: 16 semanas)

|   |     |   |             |            |             |         |   |   |  |   |               |         |
|---|-----|---|-------------|------------|-------------|---------|---|---|--|---|---------------|---------|
| 5 estudios (9-13) para dosis 150 mg y 1 estudio (9) para dosis 300 mg | ECA | Incierto en uno de los ECA (Pavelka, el único con dosis de 300) | no es serio | Es directa | no es serio | a, b, c | Dosis 150 mg: 751<br><br>Dosis 300 mg: 76 | Dosis 150 mg: 602<br><br>Dosis 300 mg: 76 | SEC 150 mg: RR 1,39 (1,25 a 1,56)<br><br>SEC 300 mg: RR 1,64 (1,16 a 2,32) | SEC 150 mg: 166 más por mil (de 104 a 235 más)<br><br>SEC 300 mg: 237 más por mil (de 60 a 487 más) | ⊕⊕⊕○ MODERADA | crítica |
|---|-----|---|-------------|------------|-------------|---------|---|---|--|---|---------------|---------|

ASAS40 (seguimiento: 16 semanas)

| Evaluación de certeza   |                   |                                      |                |                     |             |                       | Número de pacientes                       |   | Efecto   |   | Certeza       | Importancia |
|---|-------------------|--------------------------------------|----------------|---------------------|-------------|-----------------------|---|---|--|---|---------------|-------------|
| Nº de estudios  | Diseño de estudio | Riesgo de sesgo                      | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Secukinumab                               | Placebo                                   | Relativo (95% IC)  | Absoluto (95% IC)   |               |             |
| 5 estudios (9-13) para dosis 150 mg y 1 estudio (9) para dosis 300 mg | ECA               | Incierto en uno de los ECA (Pavelka) | no es serio    | Es directa          | no es serio | a, b, c               | Dosis 150 mg: 751<br><br>Dosis 300 mg: 76 | Dosis 150 mg: 602<br><br>Dosis 300 mg: 76 | SEC 150 mg: RR 1,76 (1,49 a 2,08)<br><br>SEC 300 mg: RR 1,74 (1,05 a 2,87) | SEC 150 mg: 180 más por mil (de 116 a 255 más)<br><br>SEC 300 mg: 179 más por mil (de 12 a 452 más) | ⊕⊕⊕○ MODERADA | critica     |

#### BASDAI50 (seguimiento: 16 semanas)

|                     |     |             |             |            |             |      |             |     |                       |                                   |               |            |
|---------------------|-----|-------------|-------------|------------|-------------|------|-------------|-----|-----------------------|-----------------------------------|---------------|------------|
| 2 estudios: (12,13) | ECA | no es serio | no es serio | Es directa | no es serio | a, c | 150 mg: 255 | 256 | RR 1,68 (1,26 a 2,23) | 146 más por mil (de 56 a 265 más) | ⊕⊕⊕○ MODERADA | importante |
|---------------------|-----|-------------|-------------|------------|-------------|------|-------------|-----|-----------------------|-----------------------------------|---------------|------------|

#### BASFI (mejoría media) a las 16 semanas

|                |     |             |    |            |             |  |     |     |         |  |           |            |
|----------------|-----|-------------|----|------------|-------------|--|-----|-----|---------|--|-----------|------------|
| 1 estudio (12) | ECA | No es serio | NA | Es directa | No es serio | Reportado como variable continua, sin punto de corte | 184 | 186 | P=0,014 | SEC: -1,64 (0,20)<br><br>PBO: -1,01 (0,21) | ⊕⊕⊕⊕ ALTA | importante |
|----------------|-----|-------------|----|------------|-------------|--|-----|-----|---------|--|-----------|------------|

#### ASDAS LDA a 8 semanas

|               |     |             |    |            |             |  |             |    |                       |                                   |           |            |
|---------------|-----|-------------|----|------------|-------------|--|-------------|----|-----------------------|-----------------------------------|-----------|------------|
| 1 estudio (7) | ECA | No es serio | NA | Es directa | No es serio |  | 150 mg: 285 | 90 | RR 1,89 (1,18 – 3,04) | 159 más por mil (de 32 a 363 más) | ⊕⊕⊕⊕ ALTA | importante |
|---------------|-----|-------------|----|------------|-------------|--|-------------|----|-----------------------|-----------------------------------|-----------|------------|

#### ASDAS ID a las 8 semanas

|                      |     |             |             |            |             |   |             |     |                       |                                  |           |            |
|----------------------|-----|-------------|-------------|------------|-------------|---|-------------|-----|-----------------------|----------------------------------|-----------|------------|
| 3 estudios (7,11,13) | ECA | No es serio | No es serio | Es directa | No es serio | c | 150 mg: 774 | 429 | RR 2,70 (1,77 – 4,13) | 95 más por mil (de 43 a 175 más) | ⊕⊕⊕⊕ ALTA | importante |
|----------------------|-----|-------------|-------------|------------|-------------|---|-------------|-----|-----------------------|----------------------------------|-----------|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza; SEC, Secukinumab;

**Explicaciones:**

- a. El estudio de Kiltz es en EspA radiográfica es un abstract del congreso EULAR, por eso se ha bajado la evidencia en algunos desenlaces. Tiene 2 grupos SEC con retirada temprana o retardada de AINE. Se ha cogido el grupo de retirada retardada (4 sem) por ser lo habitual en práctica clínica.
- b. Se ha bajado evidencia por incluir estudio de Kiltz (abstract congreso EULAR) y porque la aleatorización en estudio de Pavelka que no está del todo clara.
- c. El estudio de Deodhar es en EspA axial no radiográfica. Tiene dos grupos SEC, con y sin primera dosis IV. Se ha cogido el grupo de SEC sin primera dosis IV, por ser lo habitual en práctica clínica

**Referencias:**

7. Poddubnyy D, Pournara E, Zielińska A, Baranauskaite A, Jiménez AM, Sadhu S, et al. Rapid improvement in spinal pain in patients with axial spondyloarthritis treated with secukinumab: primary results from a randomized controlled phase-IIb trial. Ther Adv Musculoskelet Dis. 2021;13:1759720x211051471.
9. Pavelka K, Kivitz A, Dokoupilova E, Blanco R, Maradiaga M, Tahir H, et al. Efficacy, safety, and tolerability of secukinumab in patients with active ankylosing spondylitis: a randomized, double-blind phase 3 study, MEASURE 3. Arthritis Res Ther. 22 de diciembre de 2017;19(1):285.
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11. Huang F, Sun F, Wan WG, Wu LJ, Dong LL, Zhang X, et al. Secukinumab provided significant and sustained improvement in the signs and symptoms of ankylosing spondylitis: results from the 52-week, Phase III China-centric study, MEASURE 5. Chin Med J (Engl). 5 de noviembre de 2020;133(21):2521-31.
12. Kiltz U, Baraliakos X, Brandt-Juergens J, Wagner U, Lieb S, Sieder C, et al. Evaluation of the nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with ankylosing spondylitis: results of the multicenter, randomised, double-blind, phase iv astrumtrial. Ann Rheum Dis. 2021;80(SUPPL 1):714-715.
13. Deodhar A, Blanco R, Dokoupilová E, Hall S, Kameda H, Kivitz AJ, et al. Improvement of Signs and Symptoms of Nonradiographic Axial Spondyloarthritis in Patients Treated With Secukinumab: Primary Results of a Randomized, Placebo-Controlled Phase III Study. Arthritis Rheumatol Hoboken NJ. 2021;73(1):110-20.

## Secukinumab vs placebo en manifestaciones axiales de la artritis psoriásica

**Pregunta:** Secukinumab 150 mg y 300 mg/ 4 semanas comparado con placebo para manifestaciones axiales de la artritis psoriásica

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Secukinumab     | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

ASAS20 (seguimiento: 12 semanas)

|        |     |             |    |            |             |  |  |     |  |  |           |         |
|--------|-----|-------------|----|------------|-------------|--|--|-----|--|--|-----------|---------|
| 1 (25) | ECA | no es serio | NA | Es directa | no es serio |  | SEC 300 mg: 167 ptes<br><br>SEC 150 mg: 165 ptes | 166 | SEC 150 mg: RR 2,15 (1,67 a 2,77)<br><br>SEC 300 mg: RR 2,02 (1,56 a 2,61) | SEC 150 mg: 353 más por mil (de 206 a 544 más)<br><br>SEC 300 mg: 317 más por mil (de 175 a 501 más) | ⊕⊕⊕⊕ ALTA | crítica |
|--------|-----|-------------|----|------------|-------------|--|--|-----|--|--|-----------|---------|

ASAS40 (seguimiento: 12 semanas)

|        |     |             |    |            |             |  |  |     |  |  |           |         |
|--------|-----|-------------|----|------------|-------------|--|--|-----|--|--|-----------|---------|
| 1 (25) | ECA | no es serio | NA | Es directa | no es serio |  | SEC 300 mg: 167 ptes<br><br>SEC 150 mg: 165 ptes | 166 | SEC 150 mg: RR 3,20 (2,03 a 5,04)<br><br>SEC 300 mg: RR 3,55 (2,27 a 5,54) | SEC 150 mg: 273 más por mil (de 128 a 502 más)<br><br>SEC 300 mg: 317 más por mil (de 158 a 564 más) | ⊕⊕⊕⊕ ALTA | critica |
|--------|-----|-------------|----|------------|-------------|--|--|-----|--|--|-----------|---------|

BASDAI50 (seguimiento: 12 semanas)

| Evaluación de certeza |                   |                 |                |                     |             |                       | Número de pacientes                              |         | Efecto   |  | Certeza   | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|--|---------|--|--|-----------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Secukinumab                                      | Placebo | Relativo (95% IC)  | Absoluto (95% IC)  |           |             |
| 1 (25)                | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | SEC 300 mg: 167 ptes<br><br>SEC 150 mg: 165 ptes | 166     | SEC 150 mg: RR 3,59 (2,03 a 5,69)<br><br>SEC 300 mg: RR 3,81 (2,30 a 6,32) | SEC 150 mg: 234 más por mil (de 100 a 457 más)<br><br>SEC 300 mg: 274 más por mil (de 127 a 519 más) | ⊕⊕⊕⊕ ALTA | importante  |

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza;; SEC, Secukinumab; NA, no aplica

#### Referencias:

25. Baraliakos X, Gossec L, Pournara E, Jeka S, Mera-Varela A, D'Angelo S, et al. Secukinumab in patients with psoriatic arthritis and axial manifestations: results from the double-blind, randomised, phase 3 MAXIMISE trial. Ann Rheum Dis. 2021;80(5):582-90

## Ixekizumab vs placebo en espondiloartritis axial

**Pregunta:** Ixekizumab 80 mg/4 semanas comparado con placebo para espondiloartritis axial

| Evaluación de certeza                      |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto                 |                                   | Certeza     | Importancia |
|--|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|------------------------|-----------------------------------|-------------|-------------|
| Nº de estudios                             | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Ixekizumab      | Placebo | Relativo (95% CI)      | Absoluto (95% CI)                 |             |             |
| <b>ASAS20 (seguimiento 16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |                        |                                   |             |             |
| 2 (14,15)                                  | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a                     | 195             | 191     | RR 1,59 (1,26 a 2,00)  | 203 más por mil (de 89 a 347 más) | ⊕⊕⊕ ALTA    | crítica     |
| <b>ASAS40 (seguimiento 16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |                        |                                   |             |             |
| 3 (14–16)                                  | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a                     | 291             | 296     | RR 2,12 (1,57 a 2,86)  | 185 más por mil (de 94 a 308 más) | ⊕⊕⊕ ALTA    | crítica     |
| <b>BASDAI50 (seguimiento: 16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |                        |                                   |             |             |
| 3 (14–16)                                  | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a                     | 291             | 296     | RR 2,26 (1,62 a 3,17)  | 171 más por mil (de 83 a 293 más) | ⊕⊕⊕ ALTA    | importante  |
| <b>ASDAS LDA (seguimiento: 16 semanas)</b> |                   |                 |                |                     |             |                       |                 |         |                        |                                   |             |             |
| 3 (14–16)                                  | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a                     | 291             | 296     | RR 2,88 (1,94 a 4,25)  | 184 más por mil (de 93 a 319 más) | ⊕⊕⊕ ALTA    | importante  |
| <b>ASDAS ID (seguimiento: 16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |                        |                                   |             |             |
| 2 (14,15)                                  | ECA               | no es serio     | No es serio    | Es directa          | No es serio | a, b                  | 195             | 191     | RR 5,55 (1,65 a 18,63) | 71 más por mil (de 10 a 277 más)  | ⊕⊕ MODERADA | importante  |

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Ixekizumab      | Placebo | Relativo (95% CI) | Absoluto (95% CI) |         |             |

#### ASDAS MI (seguimiento: 16 semanas)

|           |     |             |             |            |             |   |     |     |                        |                                   |          |            |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|------------------------|-----------------------------------|----------|------------|
| 2 (14,15) | ECA | no es serio | No es serio | Es directa | no es serio | a | 195 | 191 | RR 5,14 (2,48 a 10,66) | 173 más por mil (de 62 a 405 más) | ⊕⊕⊕ ALTA | importante |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|------------------------|-----------------------------------|----------|------------|

#### ASDAS CII (seguimiento: 16 semanas)

|           |     |             |             |            |             |   |     |     |                       |                                    |          |            |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|-----------------------|------------------------------------|----------|------------|
| 2 (14,15) | ECA | no es serio | No es serio | Es directa | no es serio | a | 195 | 191 | RR 2,47 (1,82 a 3,36) | 309 más por mil (de 172 a 495 más) | ⊕⊕⊕ ALTA | importante |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|-----------------------|------------------------------------|----------|------------|

#### BASFI (seguimiento 16 semanas)

|  |  |  |  |  |  |  |  |  |  |  |  |            |
|--|--|--|--|--|--|--|--|--|--|--|--|------------|
|  |  |  |  |  |  | Reportado como variable continua, sin punto de corte |  |  |  |  |  | importante |
|--|--|--|--|--|--|--|--|--|--|--|--|------------|

#### PCR (seguimiento 16 semanas)

|  |  |  |  |  |  |  |  |  |  |  |  |            |
|--|--|--|--|--|--|--|--|--|--|--|--|------------|
|  |  |  |  |  |  | Reportado como variable continua, sin punto de corte |  |  |  |  |  | importante |
|--|--|--|--|--|--|--|--|--|--|--|--|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza; NA, no aplica; IXE, ixekizumab

#### Explicaciones:

- a. Los tres estudios incluidos tienen un brazo de ixekizumab cada 4 semanas y otro cada 2 semanas. Para las comparaciones se ha utilizado la dosis de 80 mg/4 sem porque es la que se utiliza en la práctica clínica,
- b. Alta imprecisión (gran intervalo de confianza) por el bajo número de pacientes que alcanzan el desenlace. Se ha bajado la certeza por ello aunque no se considera serio el riesgo de imprecisión porque ambos límites del intervalo de confianza están del mismo lado.

#### Referencias:

14. van der Heijde D, Cheng-Chung Wei J, Dougados M, Mease P, Deodhar A, Maksymowych WP, et al. Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. Lancet Lond Engl. 8 de diciembre de 2018;392(10163):2441-51.
15. Deodhar A, Poddubnyy D, Pacheco-Tena C, Salvarani C, Lespessailles E, Rahman P, et al. Efficacy and Safety of Ixekizumab in the Treatment of Radiographic Axial Spondyloarthritis: Sixteen-Week Results From a Phase III Randomized, Double-Blind, Placebo-Controlled Trial in Patients With Prior Inadequate Response to or Intolerance of Tumor Necrosis Factor Inhibitors. Arthritis Rheumatol Hoboken NJ. abril de 2019;71(4):599-611.
16. Deodhar A, van der Heijde D, Gensler LS, Kim TH, Maksymowych WP, Østergaard M, et al. Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial. Lancet Lond Engl. 4 de enero de 2020;395(10217):53-64.

## Brodalumab vs placebo en espondiloartritis axial

**Pregunta:** Brodalumab 210 mg/2 semanas comparado con placebo para espondiloartritis axial

| Evaluación de certeza                      |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto                |  | Certeza   | Importancia |
|--|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-----------------------|--|-----------|-------------|
| Nº de estudios                             | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Brodalumab      | Placebo | Relativo (95% IC)     | Absoluto (95% IC)                        |           |             |
| <b>ASAS20 (seguimiento 16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |                       |  |           |             |
| 1 (17)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 80              | 79      | RR 1,62 (1,20 a 2,18) | 257 más por mil (de 82 a 495 más)        | ⊕⊕⊕⊕ ALTA | crítica     |
| <b>ASAS40 (seguimiento 16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |                       |  |           |             |
| 1 (17)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 80              | 79      | RR 1,82 (1,14 a 2,89) | 197 más por mil (de 35 a 455 más)        | ⊕⊕⊕⊕ ALTA | crítica     |
| <b>ASDAS LDA (seguimiento: 16 semanas)</b> |                   |                 |                |                     |             |                       |                 |         |                       |  |           |             |
| 1 (17)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 80              | 79      | RR 0,99 (0,60 a 1,63) | 3 menos por mil (de 112 menos a 176 más) | ⊕⊕⊕⊕ ALTA | importante  |
| <b>ASDAS ID (seguimiento: 16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |                       |  |           |             |
| 1 (17)                                     | ECA               | no es serio     | NA             | Es directa          | No es serio |                       | 80              | 79      | RR 1,67 (1,11 a 2,53) | 196 más por mil (de 32 a 444 más)        | ⊕⊕⊕⊕ ALTA | importante  |
| <b>ASDAS MI (seguimiento: 16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |                       |  |           |             |
| 1 (17)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 80              | 79      | RR 2,37 (0,88 a 6,42) | 87 más por mil (de 8 menos a 343 más)    | ⊕⊕⊕⊕ ALTA | importante  |

| Evaluación de certeza |                   |                 |                |                     |             |                       | Número de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|---------------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Brodalumab          | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

**ASDAS CII (seguimiento: 16 semanas)**

|        |     |             |    |            |             |  |    |    |                       |                                  |           |            |
|--------|-----|-------------|----|------------|-------------|--|----|----|-----------------------|----------------------------------|-----------|------------|
| 1 (17) | ECA | no es serio | NA | Es directa | no es serio |  | 80 | 79 | RR 1,63 (1,03 a 2,58) | 159 más por mil (de 7 a 400 más) | ⊕⊕⊕⊕ ALTA | importante |
|--------|-----|-------------|----|------------|-------------|--|----|----|-----------------------|----------------------------------|-----------|------------|

**BASFI (seguimiento 16 semanas)**

|        |     |             |    |            |             |  |    |    |                                  |           |            |
|--------|-----|-------------|----|------------|-------------|--|----|----|----------------------------------|-----------|------------|
| 1 (17) | ECA | No es serio | NA | Es directa | No es serio | Reportado como variable continua, sin punto de corte | 80 | 79 | BRO -1,1 (1,8)<br>PBO -0,7 (2,2) | ⊕⊕⊕⊕ ALTA | importante |
|--------|-----|-------------|----|------------|-------------|--|----|----|----------------------------------|-----------|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza; NA, no aplica

**Explicaciones:**

- No se ha incluido la siguiente referencia. Kim TH, Kishimoto M, Wei JC, Jeong H, Nozaki A, Kobayashi S. Brodalumab, an anti-interleukin-17 receptor A monoclonal antibody, in axial spondyloarthritis: 68-week results from a phase 3 study. *Rheumatol Oxf Engl*. 2022;in press. doi: 10.1093/rheumatology/keac522. El motivo es que presenta el seguimiento a 68 semanas pero los pacientes del brazo placebo están recibiendo brodalumab desde la semana 16 por lo que ya no se mantiene la comparación.

**Referencias:**

17. Wei JC, Kim TH, Kishimoto M, Ogusu N, Jeong H, Kobayashi S. Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomised, placebo-controlled, phase 3 trial. *Ann Rheum Dis*. 2021;80(8):1014-21

## Bimekizumab vs placebo en espondiloartritis axial

**Pregunta:** Bimekizumab 160 mg/ 4 semanas comparado con placebo para espondiloartritis axial

| Evaluación de certeza                         |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto                                       |  | Certeza   | Importancia |
|---|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|--|--|-----------|-------------|
| Nº de estudios                                | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Bimekizumab     | Placebo | Relativo (95% IC)                            | Absoluto (95% IC)                            |           |             |
| <b>ASAS20 (seguimiento 12-16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |  |  |           |             |
| 2 (18,28)                                     | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a, b                  | 409             | 297     | RR 1,68 (1,43 a 1,97)                        | 258 más por mil (de 162 a 370)               | ⊕⊕⊕⊕ ALTA | crítica     |
| <b>ASAS40 (seguimiento 12-16 semanas)</b>     |                   |                 |                |                     |             |                       |                 |         |  |  |           |             |
| 2 (18,28)                                     | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a, b                  | 409             | 297     | RR 2,28 (1,77 a 2,92)                        | 258 más por mil (de 156 a 388 más)           | ⊕⊕⊕⊕ ALTA | crítica     |
| <b>ASDAS MI (seguimiento: 12-16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |  |  |           |             |
| 2 (18,28)                                     | ECA               | no es serio     | No es serio    | Es directa          | no es serio | a, b                  | 409             | 297     | RR 5,23 (3,11 a 8,79)                        | 214 más por mil (de 107 a 393 más)           | ⊕⊕⊕⊕ ALTA | importante  |
| <b>ASDAS LDA (seguimiento: 12-16 semanas)</b> |                   |                 |                |                     |             |                       |                 |         |  |  |           |             |
| 2 (18,28)                                     | ECA               | no es serio     | NA             | Es directa          | Serio       | a, b                  | 60              | 60      | RR 2,13 (0,99 a 4,55)                        | 150 más por mil (de 1 menos a 473 más)       | ⊕⊕⊕⊕ ALTA | importante  |
| <b>ASDAS ID (seguimiento: 12-16 semanas)</b>  |                   |                 |                |                     |             |                       |                 |         |  |  |           |             |
| 2 (18,28)                                     | ECA               | no es serio     | NA             | Es directa          | Serio       | a, b                  | 60              | 60      | No calculable por 0 eventos en grupo placebo | No calculable por 0 eventos en grupo placebo | ⊕⊕⊕⊕ ALTA | importante  |

| Evaluación de certeza |                   |                 |                |                     |             |                       | Número de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|---------------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Bimekizumab         | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

**BASDAI50 (seguimiento: 12 semanas)**

|        |     |             |    |            |             |      |    |    |                       |                                   |           |            |
|--------|-----|-------------|----|------------|-------------|------|----|----|-----------------------|-----------------------------------|-----------|------------|
| 1 (18) | ECA | no es serio | NA | Es directa | no es serio | a, b | 60 | 60 | RR 3,29 (1,53 a 7,07) | 267 más por mil (de 61 a 708 más) | ⊕⊕⊕⊕ ALTA | importante |
|--------|-----|-------------|----|------------|-------------|------|----|----|-----------------------|-----------------------------------|-----------|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza; NA, no aplica

**Explicaciones:**

- a. Para las comparaciones se ha usado la dosis de BMK 160 mg cada 4 semanas que es la que se ha establecido posteriormente para el tratamiento de las espondiloartritis.
- b. Se han agregado los resultados de dos estudios con tiempos de seguimiento distintos (12 y 16 semanas)

**Referencias:**

18. van der Heijde D, Gensler LS, Deodhar A, Baraliakos X, Poddubnyy D, Kivitz A, et al. Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double-blind, placebo-controlled, dose-ranging study. Ann Rheum Dis. mayo de 2020;79(5):595-604.  
 28. van der Heijde D, Deodhar A, Baraliakos X, Brown MA, Dobashi H, Dougados M, et al. Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials. 2023/01/18 ed. Ann Rheum Dis. 2023.

## Netakimab vs placebo en espondiloartritis axial

**Pregunta:** Netakimab 120 mg/2 sem comparado con placebo para espondiloartritis axial

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Netakimab       | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

### ASAS20 (seguimiento 16 semanas)

|           |     |             |             |            |             |   |     |     |                        |                                     |           |         |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|------------------------|-------------------------------------|-----------|---------|
| 2 (19,33) | ECA | no es serio | No es serio | Es directa | no es serio | a | 136 | 136 | RR 7,42 (4,26 a 12,92) | 566 más por mil (de 288 a 1050 más) | ⊕⊕⊕⊕ ALTA | crítica |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|------------------------|-------------------------------------|-----------|---------|

### ASAS40 (seguimiento 16 semanas)

|           |     |             |             |            |             |   |     |     |                         |                                    |           |         |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|-------------------------|------------------------------------|-----------|---------|
| 2 (19,33) | ECA | no es serio | No es serio | Es directa | no es serio | a | 136 | 136 | RR 10,33 (4,63 a 23,08) | 412 más por mil (de 160 a 974 más) | ⊕⊕⊕⊕ ALTA | crítica |
|-----------|-----|-------------|-------------|------------|-------------|---|-----|-----|-------------------------|------------------------------------|-----------|---------|

### BASFI (seguimiento 16 semanas)

|           |     |  |  |  |  |   |  |  |  |  |  |            |
|-----------|-----|--|--|--|--|---|--|--|--|--|--|------------|
| 2 (19,33) | ECA |  |  |  |  | Reportado como variable continua, sin punto de corte en los 2 ECA |  |  |  |  |  | importante |
|-----------|-----|--|--|--|--|---|--|--|--|--|--|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza;

#### Explicaciones:

- a. Se usa dosis de netakimab 120 mg/2 semanas.

#### Referencias:

- 19. Erdes S, Nasonov E, Kunder E, Pristrom A, Soroka N, Shesternya P, et al. Primary efficacy of netakimab, a novel interleukin-17 inhibitor, in the treatment of active ankylosing spondylitis in adults. Clin Exp Rheumatol. febrero de 2020;38(1):27-34.
- 33. Mazurov VI, Gaydukova IZ, Erdes S, Dubinina TV, Pristrom AM, Kunder EV, et al. Efficacy and safety of netakimab, anti-il-17a monoclonal antibody, in patients with ankylosing spondylitis. results of phase iii international, multicenter, randomized double-blind clinical trial BCD-085-5/astera. Nauchno-Prakt Revmatol. 2020;58(4):376-86.

## Tofacitinib vs placebo en espondiloartritis axial

**Pregunta:** Tofacitinib 5 mg/12 h comparado con placebo para espondiloartritis axial

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Tofacitinib     | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

### ASAS20 (seguimiento 12-16 semanas)

|           |     |             |             |            |             |      |     |     |                       |                                    |           |         |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|---------|
| 2 (21,22) | ECA | no es serio | No es serio | Es directa | no es serio | a, b | 185 | 187 | RR 1,83 (1,44 a 2,34) | 263 más por mil (de 137 a 423 más) | ⊕⊕⊕⊕ ALTA | crítica |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|---------|

### ASAS40 (seguimiento 12-16 semanas)

|           |     |             |             |            |             |      |     |     |                       |                                    |           |         |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|---------|
| 2 (21,22) | ECA | no es serio | No es serio | Es directa | no es serio | a, b | 185 | 187 | RR 3,07 (2,07 a 4,55) | 288 más por mil (de 149 a 494 más) | ⊕⊕⊕⊕ ALTA | crítica |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|---------|

### ASDAS <2,1 (LDA+ID) (seguimiento: 12-16 semanas)

|           |     |             |             |            |             |      |     |     |                       |                                    |           |            |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|------------|
| 2 (21,22) | ECA | no es serio | No es serio | Es directa | no es serio | a, b | 185 | 187 | RR 3,85 (2,49 a 5,95) | 320 más por mil (de 167 a 556 mas) | ⊕⊕⊕⊕ ALTA | importante |
|-----------|-----|-------------|-------------|------------|-------------|------|-----|-----|-----------------------|------------------------------------|-----------|------------|

### ASDAS <1,3 (ID) (seguimiento: 12-16 semanas)

|           |     |             |             |            |       |      |     |     |                        |                             |           |            |
|-----------|-----|-------------|-------------|------------|-------|------|-----|-----|------------------------|-----------------------------|-----------|------------|
| 2 (21,22) | ECA | no es serio | No es serio | Es directa | seria | a, b | 185 | 187 | RR 4,04 (1,38 a 11,87) | 65 más por mil (de 8 a 232) | ⊕⊕⊕⊕ ALTA | importante |
|-----------|-----|-------------|-------------|------------|-------|------|-----|-----|------------------------|-----------------------------|-----------|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza;

#### Explicaciones:

- a. Para las comparaciones se ha usado la dosis de tofacitinib 5 mg/12 h, la más usada en ensayos y práctica clínica.
- b. Se han agregado los resultados de dos estudios con tiempos de seguimiento distintos (12 y 16 semanas)

#### Referencias:

- 21. van der Heijde D, Deodhar A, Wei JC, Drescher E, Fleishaker D, Hendrikx T, et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Ann Rheum Dis. agosto de 2017;76(8):1340-7.
- 22. Deodhar A, Sliwinska-Stanczyk P, Xu H, Baraliakos X, Gensler LS, Fleishaker D, et al. Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study. Ann Rheum Dis. 2021;80(8):1004-13.

## Upadacitinib vs placebo en espondiloartritis axial

**Pregunta:** Upadacitinib 15 mg/d comparado con placebo para espondiloartritis axial

| Nº de estudios                             | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Evaluación de certeza |         | Nº de pacientes        |                                    | Efecto    |            | Certeza | Importancia |
|--|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------------|---------|------------------------|------------------------------------|-----------|------------|---------|-------------|
|  |                   |                 |                |                     |             |                       | Upadacitinib          | Placebo | Relativo (95% IC)      | Absoluto (95% IC)                  |           |            |         |             |
| <b>ASAS20 (seguimiento: 14 semanas)</b>    |                   |                 |                |                     |             |                       |                       |         |                        |                                    |           |            |         |             |
| 3 (23,29,30)                               | ECA               | no es serio     | no es serio    | Es directa          | no es serio |                       | 460                   | 460     | RR 1,62 (1,43 a 1,85)  | 252 más por mil (de 173 a 343 más) | ⊕⊕⊕⊕ ALTA | crítica    |         |             |
| <b>ASAS40 (seguimiento: 14 semanas)</b>    |                   |                 |                |                     |             |                       |                       |         |                        |                                    |           |            |         |             |
| 3 (23,29,30)                               | ECA               | no es serio     | no es serio    | Es directa          | no es serio |                       | 460                   | 460     | RR 2,17 (1,78 a 2,66)  | 250 más por mil (de 166 a 353 más) | ⊕⊕⊕⊕ ALTA | critica    |         |             |
| <b>BASDAI50 (seguimiento: 14 semanas)</b>  |                   |                 |                |                     |             |                       |                       |         |                        |                                    |           |            |         |             |
| 3 (23,29,30)                               | ECA               | no es serio     | no es serio    | Es directa          | no es serio |                       | 367                   | 366     | RR 2,21 (1,73 a 2,80)  | 234 más por mil (de 143 a 350 más) | ⊕⊕⊕⊕ ALTA | importante |         |             |
| <b>ASDAS LDA (seguimiento: 14 semanas)</b> |                   |                 |                |                     |             |                       |                       |         |                        |                                    |           |            |         |             |
| 1 (29)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 211                   | 209     | RR 4,39 (2,84 a 6,76)  | 340 más por mil (de 185 a 579 más) | ⊕⊕⊕⊕ ALTA | importante |         |             |
| <b>ASDAS ID (seguimiento: 14 semanas)</b>  |                   |                 |                |                     |             |                       |                       |         |                        |                                    |           |            |         |             |
| 1 (29)                                     | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | 211                   | 209     | RR 6,69 (2,38 a 18,78) | 109 más por mil (de 26 a 340 más)  | ⊕⊕⊕⊕ ALTA | importante |         |             |

| Evaluación de certeza |                   |                 |                |                     |             |                       | Número de pacientes |         | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|---------------------|---------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Upadacitinib        | Placebo | Relativo (95% IC) | Absoluto (95% IC) |         |             |

**ASDAS MI (seguimiento: 14 semanas)**

|        |     |             |    |            |             |  |     |     |                        |                                    |          |            |
|--------|-----|-------------|----|------------|-------------|--|-----|-----|------------------------|------------------------------------|----------|------------|
| 1 (29) | ECA | no es serio | NA | Es directa | no es serio |  | 211 | 209 | RR 6,24 (3,29 a 11,82) | 251 más por mil (de 110 a 518 más) | ⊕⊕⊕ ALTA | importante |
|--------|-----|-------------|----|------------|-------------|--|-----|-----|------------------------|------------------------------------|----------|------------|

**ASDAS CII (seguimiento: 14 semanas)**

|        |     |             |    |            |             |  |     |     |                       |                                |          |            |
|--------|-----|-------------|----|------------|-------------|--|-----|-----|-----------------------|--------------------------------|----------|------------|
| 1 (29) | ECA | no es serio | NA | Es directa | no es serio |  | 211 | 209 | RR 2,82 (2,14 a 3,72) | 401 más por mil (de 251 a 598) | ⊕⊕⊕ ALTA | importante |
|--------|-----|-------------|----|------------|-------------|--|-----|-----|-----------------------|--------------------------------|----------|------------|

**BASFI (14 semanas)**

|              |     |  |  |  |  |   |  |  |  |  |  |            |
|--------------|-----|--|--|--|--|---|--|--|--|--|--|------------|
| 3 (23,29,30) | ECA |  |  |  |  | Reportado como variable continua, sin punto de corte en los 3 ECA |  |  |  |  |  | importante |
|--------------|-----|--|--|--|--|---|--|--|--|--|--|------------|

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza; NA, no aplica

**Referencias:**

23. van der Heijde D, Song IH, Pangan AL, Deodhar A, van den Bosch F, Maksymowycz WP, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled, phase 2/3 trial. Lancet Lond Engl. 7 de diciembre de 2019;394(10214):2108-17.
29. van der Heijde D, Baraliakos X, Sieper J, Deodhar A, Inman RD, Kameda H, et al. Efficacy and safety of upadacitinib for active ankylosing spondylitis refractory to biological therapy: a double-blind, randomised, placebo-controlled phase 3 trial. Vol. 81, Annals of the rheumatic diseases. 2022;81:1515-1523.
30. Deodhar A, Van den Bosch F, Poddubnyy D, Maksymowycz WP, van der Heijde D, Kim TH, et al. Upadacitinib for the treatment of active non-radiographic axial spondyloarthritis (SELECT-AXIS 2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Lond Engl. 2022;400(10349):369-79.

## Filgotinib vs placebo en espondilitis anquilosante

**Pregunta:** Filgotinib 200 mg/d comparado con placebo para espondilitis anquilosante

| Nº de estudios                          | Diseño de estudio | Evaluación de certeza |                |                     |             |                       | Nº de pacientes | Efecto     |   | Certeza  | Importancia |
|---|-------------------|-----------------------|----------------|---------------------|-------------|-----------------------|-----------------|------------|---|----------|-------------|
|   |                   | Riesgo de sesgo       | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones |                 | Filgotinib | Placebo   |          |             |
| <b>ASAS20 (seguimiento: 12 semanas)</b> |                   |                       |                |                     |             |                       |                 |            |   |          |             |
| 1 (20)                                  | ECA               | no es serio           | NA             | Es directa          | no es serio |                       | 58              | 58         | RR 1,91 (1,35 a 2,71)<br>362 más por mil (de 139 a 679 más) | ⊕⊕⊕ ALTA | crítica     |
| <b>ASAS40 (seguimiento: 12 semanas)</b> |                   |                       |                |                     |             |                       |                 |            |   |          |             |
| 1 (20)                                  | ECA               | no es serio           | NA             | Es directa          | no es serio |                       | 58              | 58         | RR 2,00 (1,07 a 3,74)<br>190 más por mil (de 13 a 519 más)  | ⊕⊕⊕ ALTA | crítica     |

ECA, ensayo clínico aleatorizado; IC: Intervalo de confianza;

### Referencias:

20. van der Heijde D, Baraliakos X, Gensler LS, Maksymowycz WP, Tseluyko V, Nadashkevich O, et al. Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active ankylosing spondylitis (TORTUGA): results from a randomised, placebo-controlled, phase 2 trial. Lancet Lond Engl. 1 de diciembre de 2018;392(10162):2378-87.

## Predictors of prognosis

### Clinical question

In axSpA, what are the predictors of response to IL-17 and JAK inhibitors?

### Sexo

| Evaluación de certeza                                |                   |                 |                |                     |             |                       | Nº de pacientes                  |                                 | Efecto  |  | Certeza                   | Importancia |
|--|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|----------------------------------|---------------------------------|---|--|---------------------------|-------------|
| Nº de estudios                                       | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Hombres                          | Mujeres                         | Relativo (95% IC)   | Absoluto (95% IC)  |                           |             |
| <b>ASAS40 (seguimiento: 16 semanas)</b>              |                   |                 |                |                     |             |                       |                                  |                                 |   |  |                           |             |
| Van der Horst-Bruinsma 2021 (4)                      | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | EspA-ax-r: 159<br>EspA-ax-nr: 50 | EspA-ax-r: 36<br>EspA-ax-nr: 46 | EspA-ax-r: RR 2,34 (1,10 – 4,98)<br>EspA-ax-nr: RR 1,92 (1,06 – 3,49) | EspA-ax-r: 223 más por mil (de 16 a 664)<br>EspA-ax-nr: 221 más por cada mil (de 14 a 596)         | ⊕⊕⊕ ALTA <sup>a</sup>     | crítica     |
| <b>ASAS40 (seguimiento: 52 semanas)</b>              |                   |                 |                |                     |             |                       |                                  |                                 |   |  |                           |             |
| Van der Horst-Bruinsma 2021 (4)                      | Extensión         | no es serio     | NA             | Es directa          | No es serio |                       | EspA-ax-r: 159<br>EspA-ax-nr: 50 | EspA-ax-r: 36<br>EspA-ax-nr: 46 | EspA-ax-r: RR 1,32 (0,81 – 2,16)<br>EspA-ax-nr: RR 0,99 (0,54 – 1,81) | EspA-ax-r: 107 más por cada mil (de -65 a 388)<br>EspA-ax-nr: 4 menos por cada mil (de -141 a 247) | ⊕⊕⊕ MODERADA <sup>b</sup> | crítica     |
| <b>ASDAS-LDA (&lt;2,1) (seguimiento: 16 semanas)</b> |                   |                 |                |                     |             |                       |                                  |                                 |   |  |                           |             |
| Van der Horst-Bruinsma 2021 (4)                      | ECA               | no es serio     | NA             | Es directa          | no es serio |                       | EspA-ax-r: 159<br>EspA-ax-nr: 49 | EspA-ax-r: 36<br>EspA-ax-nr: 45 | EspA-ax-r: RR 1,85 (0,86 – 3,98)<br>EspA-ax-nr: RR 2,49 (1,16 – 5,36) | EspA-ax-r: 143 más por cada mil (de -24 a 497)<br>EspA-ax-nr: 232 más por cada mil (de 25 a 679)   | ⊕⊕⊕ ALTA <sup>a</sup>     | crítica     |

| ASDAS-LDA (<2,1) (seguimiento: 52 semanas) |                               |             |             |            |                       |  |                |                |   |   |                            |         |
|--|-------------------------------|-------------|-------------|------------|-----------------------|--|----------------|----------------|---|---|----------------------------|---------|
| Van der Horst-Bruinsma 2021 (4)            | Extensión                     | no es serio | No es serio | Es directa | No es serio           |  | EspA-ax-nr: 49 | EspA-ax-nr: 45 | EspA-ax-nr: RR 1,22 (0,65 – 2,30)   | EspA-ax-nr: 60 más por cada mil (de -93 a 346)  | ⊕⊕⊕⊖ MODERADA <sup>b</sup> |         |
| Ramonda 2022 (6)                           | Observacional sin comparación | no es serio | No es serio | Es directa | es serio <sup>c</sup> |  | 119 (47,%)     | 130 (52,2%)    | Análisis multivariable:<br><br>ASDAS < 2,1 a los 6 m: Hombres OR 1,678 (0,795 – 3,542); p=0,174 |   | ⊕⊕⊕⊖ BAJA                  | crítica |
| ASDAS-PCR (2 estudios)                     |                               |             |             |            |                       |  |                |                |   |   |                            |         |
| Chimenti 2020 (5)<br>Basal                 | Observacional sin comparación | no es serio | es serio    | Es directa | es serio <sup>c</sup> |  | 82 (48,5%)     | 87 (51,5%)     |   | Basal: Correlación positiva con sexo femenino ( $R^2 = 0,34$ ; p = 0,06)  |                            |         |
| Ramonda 2022 (6)<br>(6,12 y 24 m)          | Observacional sin comparación | no es serio | es serio    | Es directa | es serio <sup>c</sup> |  | 119 (47,%)     | 130 (52,2%)    |   | Diferencias no significativas a los 6 y 12 meses.<br>P=0,04 a los 24 meses<br><br><u>Valores absolutos ASDAS-PCR Hombres:</u><br>6 m: 2,37 (1,7-3,2)<br>12 m: 2,0 (1,4-2,7)<br>24 m: 2,3 (1,6-3,0)<br><br><u>Valores absolutos ASDAS-PCR Mujeres:</u><br>6 m: 2,8 (2,1-3,7)<br>12 m: 2,4 (1,9-3,5)<br>24 m: 2,3 (1,6-3,0) | ⊕⊕⊕⊖ BAJA                  | crítica |

| BASDAI (3 estudios)                |                               |             |          |            |                       |  |              |               |  |  |                            |            |
|------------------------------------|-------------------------------|-------------|----------|------------|-----------------------|--|--------------|---------------|--|--|----------------------------|------------|
| Van der Horst-Bruinsma 2021 (4)    | ECA y estudio de extensión    | no es serio | es serio | Es directa | es serio <sup>c</sup> |  |              |               |  | Mayores cambios (reducción) en hombres                                       |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <b>HOMBRES</b>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <u>Cambio medio sem 16</u>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-r: -2,65 (0,16)  |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-nr: -2,69 (0,30)   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <u>Cambio medio sem 52</u>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-nr: -2,82 (0,33)   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <b>MUJERES</b>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <u>Cambio medio sem 16</u>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-r: -1,86 (0,34)  |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-nr: -1,64 (0,32)   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | <u>Cambio medio sem 52</u>   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | EspA-ax-nr: -2,20 (0,34)   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  |  | ⊕⊕⊕⊖ MODERADA <sup>b</sup> | importante |
| Chimenti 2020 (5)<br>(basal)       | Observacional sin comparación | no es serio | es serio | Es directa | es serio <sup>c</sup> |  | N=82 (48,5%) | N=87 (51,5%)  |  | Basal: Correlación negativa con sexo masculino ( $R^2 = 0,4$ ; $p = 0,002$ ) |                            |            |
| Ramonda 2022 (6)<br>(6, 12 y 24 m) | Observacional sin comparación | no es serio | es serio | Es directa | es serio <sup>c</sup> |  | N=119 (47%)  | N=130 (52,2%) | <u>Análisis multivariable:</u><br>BASDAI < 4 a los 6 m:<br>Hombres OR 2,151<br>(1,125 – 4,114);<br>$p=0,021$ | Diferencias no significativas en ningún momento del seguimiento.             |                            | ⊕⊕⊖⊖ BAJA  |
|                                    |                               |             |          |            |                       |  |              |               |  | <u>Valores absolutos BASDAI Hombres:</u>                                     |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | 6 m: 4.0 (2.6-5.5)   |                            |            |
|                                    |                               |             |          |            |                       |  |              |               |  | 12 m: 3.0 (2.0-4.2)  |                            |            |

|   |                      |             |             |            |                       |   |  |   |  |  |                           |            |
|---|----------------------|-------------|-------------|------------|-----------------------|---|--|---|--|--|---------------------------|------------|
|   |                      |             |             |            |                       |   |  |   |  | 24 m: 2.4 (1.2-3.5)  |                           |            |
|   |                      |             |             |            |                       |   |  |   |  | <u>Valores absolutos</u><br><u>BASDAI Mujeres:</u>   |                           |            |
|   |                      |             |             |            |                       |   |  |   |  | 6 m: 5.0 (3.4-6.3)   |                           |            |
|   |                      |             |             |            |                       |   |  |   |  | 12 m: 4.0 (2.8-5.6)  |                           |            |
|   |                      |             |             |            |                       |   |  |   |  | 24 m: 3.0 (2.1-4.7)  |                           |            |
| <b>mSASSS (Cambio medio) (2 estudios)</b> |                      |             |             |            |                       |   |  |   |  |  |                           |            |
| Braun 2019 (2)<br>(semana 208)            | Estudio de extensión | no es serio | No es serio | Es directa | es serio <sup>c</sup> | *imprecisión por tratarse de un grupo pequeño<br><br>*El subgrupo 75-150 cambió de dosis a la semana 156. | SEC 150 (n=45)<br><br>SEC 75 (n=43)<br><br>SEC 75-150 (n=20) | SEC 150 (n=26)<br><br>SEC 75 (n=18)<br><br>SEC 75-150 (n=3) |  | Mayores cambios en varones<br><br><b>HOMBRES</b><br><br>SEC 150: 1,5 (3,98)<br>SEC 75: 2,3 (4,89)<br>SEC 75-150: 1,8 (6,06)<br><br><b>MUJERES</b><br><br>SEC 150: 0,8 (3,8)<br>SEC 77: 0,6 (2,17)<br>SEC 75-150: 0,0 (0,0) | ⊕⊕⊕⊖<br>BAJA <sup>c</sup> | importante |
| Van der Heijde 2022 (3)<br>(2 años)       | Estudio de extensión | no es serio | No es serio | Es directa | No es serio           |   | IXE/4s (n=99)<br><br>IXE/2s (n=89)<br><br>IXE total (n=188)  | IXE/4s (n=16)<br><br>IXE/2s (n=26)<br><br>IXE total (n=42)  | Mayor cambio (más progresión) en varones<br><br><b>HOMBRES</b><br><br>IXE/4s: 0,5 (2,2)<br>IXE/2s: 0,3 (1,6) | ⊕⊕⊕⊖<br>MODERADA <sup>b</sup>  |                           |            |

|  |  |  |  |  |  |  |  |  |                       |  |  |
|--|--|--|--|--|--|--|--|--|-----------------------|--|--|
|  |  |  |  |  |  |  |  |  | IXE total: 0,4 (1,9)  |  |  |
|  |  |  |  |  |  |  |  |  | <b>MUJERES</b>        |  |  |
|  |  |  |  |  |  |  |  |  | IXE/4s: -0,4 (0,9)    |  |  |
|  |  |  |  |  |  |  |  |  | IXE/2s: 0,1 (0,4)     |  |  |
|  |  |  |  |  |  |  |  |  | IXE total: -0,1 (0,7) |  |  |

**mSASSS: % no progresores) (1 estudio)**

|  |                      |             |    |            |             |  |   |   |  |   |   |   |                               |            |
|--|----------------------|-------------|----|------------|-------------|--|---|---|--|---|---|---|-------------------------------|------------|
| Van der Heijde<br>2022 (3)<br>(2 años) | Estudio de extensión | no es serio | NA | Es directa | No es serio |  | <u>Cambio mSASSS ≤2</u><br><br>IXE/4s (n=99): 86,9%<br><br>IXE/2s (n=89): 87,6%<br><br>IXE total (n=188): 87,2% | <u>Cambio mSASSS ≤2</u><br><br>IXE/4s (n=16): 100%<br><br>IXE/2s (n=26): 100%<br><br>IXE total (n=42): 100% | <u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: RR 0,87 (0,80 – 0,94)<br><br>IXE/2s: RR 0,88 (0,81 – 0,95)<br><br>IXE total: RR 0,87 (0,83 – 0,92) | <u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: 131 menos por cada mil (de -195 a -62)<br><br>IXE/2s: 124 menos por cada mil (de -189 a -52)<br><br>IXE total: 128 menos por cada mil (de -174 a -79) | <u>Cambio mSASSS ≤0</u><br><br>IXE/4s: RR 0,76 (0,64 – 0,91)<br><br>IXE/2s: RR 0,83 (0,68 – 1,00)<br><br>IXE total: RR 0,81 (0,70 – 0,81) | <u>Cambio mSASSS ≤0</u><br><br>IXE/4s: 220 menos por cada mil (de -337 a -82)<br><br>IXE/2s: 154 menos por cada mil (de -279 a -4)<br><br>IXE total: 181 menos por cada mil (de -271 a -79) | ⊕⊕⊕⊖<br>MODERADA <sup>b</sup> | importante |
|--|----------------------|-------------|----|------------|-------------|--|---|---|--|---|---|---|-------------------------------|------------|

<sup>a</sup>Se considera evidencia alta porque estos datos proceden de un ensayo clínico todavía en fase de ciego (16 semanas).

<sup>b</sup>Se considera evidencia moderada porque procede de estudio de extensión de calidad alta en donde, aunque ya no hay ciego por ser fase abierta, se mantienen los grupos de aleatorización.

<sup>c</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## Edad

| Nº de estudios                                      | Diseño de estudio             | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión           | Otras consideraciones | Evaluación de certeza                                       |  | Nº de pacientes | Efecto   |                               | Certeza      | Importancia |            |
|---|-------------------------------|-----------------|----------------|---------------------|-----------------------|-----------------------|---|--|-----------------|--|-------------------------------|--------------|-------------|------------|
|   |                               |                 |                |                     |                       |                       | Edad > 40 años  | Edad < 40 años   |                 | Relativo (95% IC)  | Absoluto (95% IC)             |              |             |            |
| <b>ASDAS-PCR &lt; 2,1 a los 6 meses (1 estudio)</b> |                               |                 |                |                     |                       |                       |   |  |                 |  |                               |              |             |            |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       |   |  |                 | <u>Análisis multivariable:</u><br><br>Edad al inicio de los síntomas: OR 0,984 (0,959 – 1,010);<br>p=0,217   |                               | ⊕⊕⊖⊖<br>BAJA |             | Crítica    |
| <b>BASDAI &lt; 4 a los 6 meses (1 estudio)</b>      |                               |                 |                |                     |                       |                       |   |  |                 |  |                               |              |             |            |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       |   |  |                 | <u>Análisis multivariable:</u><br><br>Edad al inicio de los síntomas: OR 0,979 (0,956 – 1,002);<br>p=0,067   |                               | ⊕⊕⊖⊖<br>BAJA |             | importante |
| <b>mSASSS (Cambio medio) (1 estudio)</b>            |                               |                 |                |                     |                       |                       |   |  |                 |  |                               |              |             |            |
| Van der Heijde 2022 (3)<br>(2 años)                 | Estudio de extensión          | no es serio     | NA             | Es directa          | No es serio           |                       | IXE/4s (n=70)<br><br>IXE/2s (n=73)<br><br>IXE total (n=142) | IXE/4s (n=45)<br><br>IXE/2s (n=43)<br><br>IXE total (n=88) |                 | Mayor cambio (más progresión) en mayores de 40 años<br><br><b>EDAD &gt; 40 AÑOS</b><br><br>IXE/4s: 0,5 (2,1)<br>IXE/2s: 0,3 (1,7)<br>IXE total: 0,4 (1,9)<br><br><b>EDAD &lt; 40 AÑOS</b><br><br>IXE/4s: -0,3 (2,1)<br>IXE/2S: 0,1 (0,7) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> |              | importante  |            |

|  |                      |             |    |            |             |  |  |  |                       |  |  |
|--|----------------------|-------------|----|------------|-------------|--|--|--|-----------------------|--|--|
|  |                      |             |    |            |             |  |  |  | IXE total: -0,2 (1,6) |  |  |
| <b>mSASSS: % no progresores) (1 estudio)</b> |                      |             |    |            |             |  |  |  |                       |  |  |
| Van der Heijde<br>2022 (3)<br>(2 años)       | Estudio de extensión | no es serio | NA | Es directa | No es serio |  |  |  |                       |  |  |

<sup>a</sup>Se considera evidencia moderada porque procede de estudio de extensión de calidad alta en donde, aunque ya no hay ciego por ser fase abierta, se mantienen los grupos de aleatorización.

<sup>b</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## HLA-B27

| Evaluación de certeza                               |                               |                 |                |                     |                       |                       | Nº de pacientes   |  | Efecto  |                               | Certeza      | Importancia |
|---|-------------------------------|-----------------|----------------|---------------------|-----------------------|-----------------------|---|--|---|-------------------------------|--------------|-------------|
| Nº de estudios                                      | Diseño de estudio             | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión           | Otras consideraciones | HLA-B27 +   | HLA-B27 -  | Relativo (95% IC)   | Absoluto (95% IC)             |              |             |
| <b>ASDAS-PCR &lt; 2,1 a los 6 meses (1 estudio)</b> |                               |                 |                |                     |                       |                       |   |  |   |                               |              |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       | 102 (40,9%)   | 147 (59,1%)  | <u>Análisis multivariable:</u><br>OR 0,908 (0,441 – 1,868); p=0,792   |                               | ⊕⊕⊖⊖<br>BAJA | Crítica     |
| <b>BASDAI &lt; 4 a los 6 meses (1 estudio)</b>      |                               |                 |                |                     |                       |                       |   |  |   |                               |              |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       | 102 (40,9%)   | 147 (59,1%)  | <u>Análisis multivariable:</u><br>OR 0,983 (0,513 – 1,883); p=0,958   |                               | ⊕⊕⊖⊖<br>BAJA | importante  |
| <b>mSASSS (Cambio medio) (1 estudio)</b>            |                               |                 |                |                     |                       |                       |   |  |   |                               |              |             |
| Van der Heijde 2022 (3)<br>(2 años)                 | Estudio de extensión          | no es serio     | NA             | Es directa          | No es serio           |                       | IXE/4s (n=101)<br><br>IXE/2s (n=100)<br><br>IXE total (n=201) | IXE/4s (n=14)<br><br>IXE/2s (n=15)<br><br>IXE total (n=29) | Mayor cambio (más progresión) en HLA-B27+<br><br><b>HLA-B27 +</b><br>IXE/4s: 0,5 (2,2)<br>IXE/2s: 0,3 (1,5)<br>IXE total: 0,4 (1,9)<br><br><b>HLA-B27-</b><br>IXE/4s: -0,1 (0,6)<br>IXE/2s: -0,03 (0,5)<br>IXE total: -0,04 (0,5) | ⊕⊕⊖⊖<br>MODERADA <sup>a</sup> | importante   |             |
|   |                               |                 |                |                     |                       |                       |   |  |   |                               |              |             |

| mSASSS: % no progresores) (1 estudio)  |                      |             |    |            |             |  |  |  |  |   |  |
|--|----------------------|-------------|----|------------|-------------|--|--|--|--|---|--|
| Van der Heijde<br>2022 (3)<br>(2 años) | Estudio de extensión | no es serio | NA | Es directa | No es serio |  | <u>Cambio mSASSS <math>\leq 2</math></u> | <u>Cambio mSASSS <math>\leq 2</math></u> | <u>Cambio mSASSS &lt;2</u>               | <u>Cambio mSASSS &lt;2</u>                        |  |
|  |                      |             |    |            |             |  | IXE/4s (n=101):<br>87,1%                 | IXE/4s (n=14):<br>100%                   | IXE/2s: RR 0,89 (0,83 – 0,95)            | IXE/4s: 129 menos por cada mil (de -192 a -61)    |  |
|  |                      |             |    |            |             |  | IXE/2s (n=100):<br>89%                   | IXE/2s (n=15):<br>100%                   | IXE total: RR 0,88 (0,84 – 0,93)         | IXE total: 119 menos por cada mil (de -163 a -73) | $\oplus\oplus\ominus$<br>MODERADA <sup>a</sup> |
|  |                      |             |    |            |             |  | IXE total (n=201):<br>88,1%              | IXE total (n=29):<br>100%                | <u>Cambio mSASSS <math>\leq 0</math></u> | <u>Cambio mSASSS <math>\leq 0</math></u>          |  |
|  |                      |             |    |            |             |  | IXE/4s (n=101):<br>73,3%                 | IXE/4s (n=14):<br>85,7%                  | IXE/4s: RR 0,85 (0,67 – 1,09)            | IXE/4s: 124 menos por cada mil (de -283 a 78)     | importante                                     |
|  |                      |             |    |            |             |  | IXE/2s (n=100):<br>74%                   | IXE/2s (n=115):<br>93,3%                 | IXE/2s: RR 0,79 (0,66 – 0,95)            | IXE/2s: 193 menos por cada mil (de -314 a -49)    |  |
|  |                      |             |    |            |             |  | IXE total (n=201):<br>73,6%              | IXE total (n=29):<br>89,7%               | IXE total: RR 0,82 (0,71 – 0,95)         | IXE total: 173 menos por cada mil (de -262 a -71) |  |

<sup>a</sup>Se considera evidencia moderada porque procede de estudio de extensión de calidad alta en donde, aunque ya no hay ciego por ser fase abierta, se mantienen los grupos de aleatorización.

<sup>b</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## Tabaco

| Nº de estudios                                      | Diseño de estudio             | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión           | Otras consideraciones   | Nº de pacientes                     |                                     | Efecto   |  | Certeza     | Importancia |
|---|-------------------------------|-----------------|----------------|---------------------|-----------------------|---|-------------------------------------|-------------------------------------|--|--|-------------|-------------|
|   |                               |                 |                |                     |                       |   | Fumador                             | No fumador                          | Relativo (95% IC)  | Absoluto (95% IC)  |             |             |
| <b>ASDAS-PCR a los 6 meses (1 estudio)</b>          |                               |                 |                |                     |                       |   |                                     |                                     |  |  |             |             |
| Chimenti 2020 (5)                                   | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>a</sup> |   | 33 (19,5%)                          | 136 (80,5%)                         |  | Reducción a los 6 m: Correlación positiva con ser fumador ( $R^2 = 0,42$ ; $p = 0,03$ )                                | ⊕⊕⊖<br>BAJA | crítica     |
| <b>ASDAS-PCR &lt; 2,1 a los 6 meses (1 estudio)</b> |                               |                 |                |                     |                       |   |                                     |                                     |  |  |             |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>a</sup> |   | 85 (34,1%)                          | 164 (65,9%)                         | Análisis multivariable:<br>OR 0,910 (0,437 – 1,893); $p=0,800$ |  | ⊕⊕⊖<br>BAJA | crítica     |
| <b>BASDAI &lt; 4 a los 6 meses (1 estudio)</b>      |                               |                 |                |                     |                       |   |                                     |                                     |  |  |             |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>a</sup> |   | 85 (34,1%)                          | 164 (65,9%)                         | Análisis multivariable:<br>OR 1,306 (0,691 – 2,468); $p=0,411$ |  | ⊕⊕⊖<br>BAJA | importante  |
| <b>mSASSS (Cambio medio) (2 estudios)</b>           |                               |                 |                |                     |                       |   |                                     |                                     |  |  |             |             |
| Braun 2019 (2) (semana 208)                         | Estudio de extensión          | no es serio     | NA             | Es directa          | es serio <sup>a</sup> | *imprecisión por tratarse de un grupo pequeño<br><br>*El subgrupo 75-150 cambió de dosis a la semana 156. | SEC 150 (n=21)<br><br>SEC 75 (n=24) | SEC 150 (n=50)<br><br>SEC 75 (n=37) |  | Mayores cambios en fumadores<br><br>FUMADOR<br><br>SEC 150: 0,9 (1,94)<br>SEC 75: 2,0 (4,32)<br>SEC 75-150: 3,8 (6,86) | ⊕⊕⊖<br>BAJA | importante  |

|  |                      |             |    |            |             |  |  |  |   |  |  |
|--|----------------------|-------------|----|------------|-------------|--|--|--|---|--|--|
|  |                      |             |    |            |             |  |  |  | NO FUMAODR<br>SEC 150: 1,4 (4,49)<br>SEC 75: 1,6 (4,38)<br>SEC 75-150: 0,4 (4,78) |  |  |
| Van der Heijde<br>2022 (3)<br>(2 años) | Estudio de extensión | no es serio | NA | Es directa | No es serio |  |  |  | OR 2.89 (1.05–7.95);<br>$p=0,04$  |  |  |

<sup>a</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## VSG

| Nº de estudios                                     | Diseño de estudio             | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión           | Otras consideraciones | Nº de pacientes                          | Efecto            |  | Certeza  | Importancia |
|--|-------------------------------|-----------------|----------------|---------------------|-----------------------|-----------------------|--|-------------------|--|----------|-------------|
|  |                               |                 |                |                     |                       |                       |  | Relativo (95% IC) | Absoluto (95% IC)  |          |             |
| <b>ASDAS-PCR basal (1 estudio)</b>                 |                               |                 |                |                     |                       |                       |  |                   |  |          |             |
| Chimenti 2020 (5)<br>Basal                         | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>a</sup> |                       | 169 pacientes: VSG media $19,8 \pm 17,9$ |                   | Basal: Correlación positiva con VSG elevada ( $R^2 = 0,34$ ; $p = 0,004$ ) | ⊕⊕⊖ BAJA | crítica     |
| <b>BASDAI. Reducción a los 6 meses (1 estudio)</b> |                               |                 |                |                     |                       |                       |  |                   |  |          |             |
| Chimenti 2020 (5)                                  | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>a</sup> |                       | 169 pacientes: VSG media $19,8 \pm 17,9$ |                   | Correlación positiva con VSG elevada ( $R^2 = 0,65$ ; $p = 0,04$ )         | ⊕⊕⊖ BAJA | importante  |

<sup>a</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## PCR

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |             | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|-------------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | PCR normal      | PCR elevada | Relativo (95% IC) | Absoluto (95% IC) |         |             |

### ASAS20 semana 16 (1 estudio)

|  |                      |             |    |            |             |  |  |   |  |  |                               |         |
|--|----------------------|-------------|----|------------|-------------|--|--|---|--|--|-------------------------------|---------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 51,8%<br>PBO (n=102): 29,4% | SEC 150 (n=87): 72,4%<br>PBO (n=93): 28%    | SEC 150: RR 0,72 (0,57 – 0,89)<br>PBO: RR 1,05 (0,68 – 1,64) | SEC 150: 206 menos por cada mil (de -309 a -77)<br>PBO: 15 más por cada mil (de -91 a 179) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 72,1%<br>PBO (n=28): 35,7%  | SEC 150 (n=57): 33,3%<br>PBO (n=165): 27,9% | SEC 150: RR 2,16 (1,48 – 3,17)<br>PBO: RR 1,28 (0,74 – 2,23) | SEC 150: 388 más por cada mil (de 159 a 723)<br>PBO: 78 más por cada mil (de -74 a 343)    |                               |         |

### ASAS20 semana 156 (1 estudio)

|  |                      |             |    |            |             |  |                        |                       |                       |  |                               |         |
|--|----------------------|-------------|----|------------|-------------|--|------------------------|-----------------------|-----------------------|--|-------------------------------|---------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 63%   | SEC 150 (n=87): 83,3% | RR 0,76 (0,64 – 0,90) | 200 menos por cada mil (de -300 a -82) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 77,8% | SEC 150 (n=57): 56,2% | RR 1,39 (1,08 – 1,77) | 217 más por cada mil (de 47 a 434)     |                               |         |

### ASAS40 semana 16 (1 estudio)

|                |                      |             |    |            |             |  |                        |                       |                                |   |                               |         |
|----------------|----------------------|-------------|----|------------|-------------|--|------------------------|-----------------------|--------------------------------|---|-------------------------------|---------|
| Braun 2018 (1) | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 33,6% | SEC 150 (n=87): 47,1% | SEC 150: RR 0,71 (0,51 – 1,01) | SEC 150: 135 menos por cada mil (de -233 a 3) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
|----------------|----------------------|-------------|----|------------|-------------|--|------------------------|-----------------------|--------------------------------|---|-------------------------------|---------|

|  |                      |             |    |            |             |   |   |  |   |  |  |
|--|----------------------|-------------|----|------------|-------------|---|---|--|---|--|--|
| Según PCR basal < o > 10 mg/l                        |                      |             |    |            |             | PBO (n=102): 9,8%                           | PBO (n=93): 15,1%                           | PBO: RR 0,60 (0,28 – 1,30)                                   | PBO: 60 menos por cada mil (de -108 a 44)   |  |  |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio | SEC 150 (n=140): 49,3%<br>PBO (n=28): 14,3% | SEC 150 (n=57): 15,8%<br>PBO (n=165): 12,1% | SEC 150: RR 3,12 (1,67 – 5,82)<br>PBO: RR 1,18 (0,44 – 3,19) | SEC 150: 335 más por cada mil (de 107 a 761)<br>PBO: 22 más por cada mil (de -68 a 266) |  |  |

**ASAS40 semana 156 (1 estudio)**

|  |                      |             |    |            |             |                        |                       |                       |   |                               |         |
|--|----------------------|-------------|----|------------|-------------|------------------------|-----------------------|-----------------------|---|-------------------------------|---------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio | SEC 150 (n=110): 44,5% | SEC 150 (n=87): 70,3% | RR 0,64 (0,49 – 0,82) | 256 menos por cada mil (de -354 a -129) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio | SEC 150 (n=140): 64,1% | SEC 150 (n=57): 32,3% | RR 2,04 (1,36 – 3,04) | 327 más por cada mil (de 114 a 645)     |                               |         |

**BASDAI cambio medio semana 16 (1 estudio)**

|  |                      |             |    |            |             |  |   |  |  |                               |            |
|--|----------------------|-------------|----|------------|-------------|--|---|--|--|-------------------------------|------------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio | SEC 150 (n=110): - 1,99<br>PBO (n=102): - 0,86 | SEC 150 (n=87): - 2,78<br>PBO (n=93): - 0,62  |  | En el grupo tratamiento, mayor reducción del BASDAI en pacientes con PCR basal elevada       | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | importante |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio | SEC 150 (n=140): - 2,69<br>PBO (n=28): - 0,60  | SEC 150 (n=57): - 1,34<br>PBO (n=165): - 0,78 |  | En el grupo tratamiento, mayor reducción del BASDAI en pacientes que redujeron la PCR un 50% |                               |            |

**BASDAI cambio medio semana 156 (1 estudio)**

|  |                      |             |    |            |             |  |                         |                        |  |   |                           |            |
|--|----------------------|-------------|----|------------|-------------|--|-------------------------|------------------------|--|---|---------------------------|------------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): - 2,73 | SEC 150 (n=87): - 3,62 |  | Mayor reducción del BASDAI en pacientes con PCR basal elevada       | ⊕⊕⊕ MODERADA <sup>a</sup> | importante |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): - 3,42 | SEC 150 (n=57): - 2,22 |  | Mayor reducción del BASDAI en pacientes que redujeron la PCR un 50% |                           |            |

**BASDAI < 4 a los 6 meses (1 estudio)**

|                  |                               |             |    |            |                       |  |  |  |   |  |          |            |
|------------------|-------------------------------|-------------|----|------------|-----------------------|--|--|--|---|--|----------|------------|
| Ramonda 2022 (6) | Observacional sin comparación | no es serio | NA | Es directa | es serio <sup>b</sup> |  |  |  | <u>Análisis multivariable:</u><br>OR 1,011 (0,993 – 1,030); p=0,222 |  | ⊕⊕⊕ BAJA | importante |
|------------------|-------------------------------|-------------|----|------------|-----------------------|--|--|--|---|--|----------|------------|

**BASDAI50 semana 16 (1 estudio)**

|  |                      |             |    |            |             |  |   |  |  |   |                           |            |
|--|----------------------|-------------|----|------------|-------------|--|---|--|--|---|---------------------------|------------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 30%<br>PBO (n=102): 10,8%  | SEC 150 (n=87): 41,4%<br>PBO (n=93): 7,5%  | SEC 150: RR 0,73 (0,50 – 1,06)<br>PBO: RR 1,43 (0,58 – 3,54) | SEC 150: 114 menos por cada mil (de -209 a 25)<br>PBO: 33 más por cada mil (de -32 a 191) | ⊕⊕⊕ MODERADA <sup>a</sup> | importante |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 42,1%<br>PBO (n=28): 10,7% | SEC 150 (n=57): 17,5%<br>PBO (n=165): 9,1% | SEC 150: RR 2,40 (1,32 – 4,36)<br>PBO: RR 1,18 (0,36 – 3,81) | SEC 150: 246 más por cada mil (de 57 a 589)<br>PBO: 16 más por cada mil (de -58 a 255)    |                           |            |

**BASDAI50 semana 156 (1 estudio)**

|                |                      |             |    |            |             |  |                      |                       |                       |  |                           |            |
|----------------|----------------------|-------------|----|------------|-------------|--|----------------------|-----------------------|-----------------------|--|---------------------------|------------|
| Braun 2018 (1) | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 46% | SEC 150 (n=87): 61,8% | RR 0,75 (0,58 – 0,97) | 157 menos por cada mil (de -263 a -20) | ⊕⊕⊕ MODERADA <sup>a</sup> | importante |
|----------------|----------------------|-------------|----|------------|-------------|--|----------------------|-----------------------|-----------------------|--|---------------------------|------------|

|  |                      |             |    |            |             |  |                        |                       |                       |                                    |  |  |
|--|----------------------|-------------|----|------------|-------------|--|------------------------|-----------------------|-----------------------|------------------------------------|--|--|
| Según PCR basal < o > 10 mg/l                        |                      |             |    |            |             |  |                        |                       |                       |                                    |  |  |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 60,8% | SEC 150 (n=57): 33,1% | RR 1,81 (1,23 – 2,69) | 274 más por cada mil (de 78 a 564) |  |  |

ASDAS-ID semana 16 (1 estudio)

|  |                      |             |    |            |             |  |   |   |   |   |                               |         |
|--|----------------------|-------------|----|------------|-------------|--|---|---|---|---|-------------------------------|---------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 20%<br>PBO (n=102): 4,9% | SEC 150 (n=87): 12,6%<br>PBO (n=93): 1,1% | SEC 150: RR 1,58 (0,81 – 3,08)<br>PBO: RR 4,56 (0,54 – 38,31) | SEC 150: 74 más por cada mil (de -24 a 263)<br>PBO: 38 más por cada mil (de -5 a 401) | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 21,4%<br>PBO (n=28): 0%  | SEC 150 (n=57): 5,3%<br>PBO (n=165): 3,6% | SEC 150: RR 4,07 (1,29 – 12,81)<br>PBO: RR 0                  | SEC 150: 162 más por cada mil (de 15 a 622)<br>PBO: 36 menos por cada mil             |                               |         |

ASDAS-ID semana 156 (1 estudio)

|  |                      |             |    |            |             |  |                        |                       |                       |                                    |                               |         |
|--|----------------------|-------------|----|------------|-------------|--|------------------------|-----------------------|-----------------------|------------------------------------|-------------------------------|---------|
| Braun 2018 (1)<br>Según PCR basal < o > 10 mg/l      | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=110): 28,9% | SEC 150 (n=87): 15,6% | RR 1,81 (1,03 – 3,17) | 130 más por cada mil (de 5 a 349)  | ⊕⊕⊕⊖<br>MODERADA <sup>a</sup> | crítica |
| Braun 2018 (1)<br>Según descenso 50% PCR en semana 4 | Análisis post-hoc EC | No es serio | NA | Es directa | No es serio |  | SEC 150 (n=140): 25,3% | SEC 150 (n=57): 16,6% | RR 1,58 (0,81 – 3,08) | 92 más por cada mil (de -29 a 328) |                               |         |

ASDAS-PCR < 2,1 a los 6 meses (1 estudio)

|                  |                               |             |    |            |                       |  |  |  |   |  |           |         |
|------------------|-------------------------------|-------------|----|------------|-----------------------|--|--|--|---|--|-----------|---------|
| Ramonda 2022 (6) | Observacional sin comparación | no es serio | NA | Es directa | es serio <sup>b</sup> |  |  |  | <u>Análisis multivariable:</u><br>OR 3,938 (1,872–8,282); p=0,001 |  | ⊕⊕⊕⊕ BAJA | crítica |
|------------------|-------------------------------|-------------|----|------------|-----------------------|--|--|--|---|--|-----------|---------|

mSASSS (Cambio medio) (1 estudio)

|                                |                      |             |    |            |                       |   |  |  |  |  |  |           |            |
|--------------------------------|----------------------|-------------|----|------------|-----------------------|---|--|--|--|--|--|-----------|------------|
| Braun 2019 (2)<br>(semana 208) | Estudio de extensión | no es serio | NA | Es directa | es serio <sup>b</sup> | *imprecisión por tratarse de un grupo pequeño<br><br>*El subgrupo 75-150 cambió de dosis a la semana 156. | PCR basal < 5 mg/l<br><br>SEC 150 (n=26) | PCR basal > 5 mg/l<br><br>SEC 150 (n=48) |  | Mayores cambios en pacientes con PCR basal elevada<br><br><b>PCR BASAL &lt; 5 mg/l</b><br><br>SEC 150: 0,2 (0,90)<br>SEC 75: 0,9 (4,23)<br>SEC 75-150: -1,8 (4,49) |  | ⊕⊕⊕⊕ BAJA | importante |
|--------------------------------|----------------------|-------------|----|------------|-----------------------|---|--|--|--|--|--|-----------|------------|

mSASSS: % no progresores) (1 estudio)

|                                     |                      |             |    |            |             |  |  |   |  |  |  |                           |            |
|-------------------------------------|----------------------|-------------|----|------------|-------------|--|--|---|--|--|--|---------------------------|------------|
| Van der Heijde 2022 (3)<br>(2 años) | Estudio de extensión | no es serio | NA | Es directa | No es serio |  | Pacientes que normalizaron PCR a los 2 años<br><br><u>Cambio mSASSS ≤2</u><br><br>IXE/4s (n=83): 88% | Pacientes que no normalizaron PCR a los 2 años<br><br><u>Cambio mSASSS ≤2</u><br><br>IXE/4s (n=32): 90,6% | <u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: RR 0,97 (0,85 – 1,11)<br><br>IXE/2s: RR 0,92 (0,83 – 1,02)<br><br>IXE total: RR 0,95 (0,87 – 1,03) | <u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: 27 menos por cada mil (de -139 a 102)<br><br>IXE/2s: 79 menos por cada mil (de -167 a 18)<br><br>IXE total: 51 menos por cada mil (de -125 a 29) |  | ⊕⊕⊕ MODERADA <sup>a</sup> | importante |
|-------------------------------------|----------------------|-------------|----|------------|-------------|--|--|---|--|--|--|---------------------------|------------|

|  |  |  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|--|--|
|  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |

<sup>a</sup>Se considera evidencia moderada porque procede de estudio de extensión de calidad alta en donde, aunque ya no hay ciego por ser fase abierta, se mantienen los grupos de aleatorización.

<sup>b</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## Inflamación en RM basal

| Evaluación de certeza                               |                               |                 |                |                     |                       |                       | Nº de pacientes  |  | Efecto   |                           | Certeza    | Importancia |
|---|-------------------------------|-----------------|----------------|---------------------|-----------------------|-----------------------|--|--|--|---------------------------|------------|-------------|
| Nº de estudios                                      | Diseño de estudio             | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión           | Otras consideraciones | Inflamación RM   | No inflamación RM  | Relativo (95% IC)  | Absoluto (95% IC)         |            |             |
| <b>ASDAS-PCR &lt; 2,1 a los 6 meses (1 estudio)</b> |                               |                 |                |                     |                       |                       |  |  |  |                           |            |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       |  |  | <u>Análisis multivariable:</u><br><br>OR 2,375 (0,442–12,753); p=0,313   |                           | ⊕⊕⊖ BAJA   | crítica     |
| <b>BASDAI &lt; 4 a los 6 meses (1 estudio)</b>      |                               |                 |                |                     |                       |                       |  |  |  |                           |            |             |
| Ramonda 2022 (6)                                    | Observacional sin comparación | no es serio     | NA             | Es directa          | es serio <sup>b</sup> |                       |  |  | <u>Análisis multivariable:</u><br><br>OR 0,314 (0,080 – 1,227); p=0,096  |                           | ⊕⊕⊖ BAJA   | importante  |
| <b>mSASSS (Cambio medio) (1 estudio)</b>            |                               |                 |                |                     |                       |                       |  |  |  |                           |            |             |
| Van der Heijde 2022 (3)<br>(2 años)                 | Estudio de extensión          | no es serio     | NA             | Es directa          | No es serio           |                       | SPARCC columna >2 sem 52<br><br>IXE/4s (n=21)<br>IXE/2s (n=20)<br>IXE total (n=41) | SPARCC columna <2 sem 52<br><br>IXE/4s (n=34)<br>IXE/2s (n=34)<br>IXE total (n=68) | Mayor cambio (más progresión) en los que tenían más inflamación en la RM tanto en la semana 16 como 52<br><br><u>SEMANA 52</u><br><br><u>SPARCC columna &gt;2 sem 52</u><br><br>IXE/4s: 1,0 (3,8)<br>IXE/2s: 0,5 (1,3)<br>IXE total: 0,8 (2,8) | ⊕⊕⊖ MODERADA <sup>a</sup> | importante |             |

|  |  |  |  |  |  |  |                  |                   |  |  |  |  |
|--|--|--|--|--|--|--|------------------|-------------------|--|--|--|--|
|  |  |  |  |  |  |  | IXE total (n=75) | IXE total (n=100) |  | SPARCC columna <2<br><br>IXE/4s: -0,1 (1,5)<br><br>IXE/2s: 0,04 (0,8)<br><br>IXE total: -0,02 (1,2)<br><br><u>SEMANA 16</u><br><br>SPARCC columna >2<br><br>IXE/4s: 0,7 (2,6)<br><br>IXE/2s: 0,1 (1,9)<br><br>IXE total: 0,4 (2,2)<br><br>SPARCC columna <2<br><br>IXE/4s: 0,1 (2,0)<br><br>IXE/2s: 0,2 (1,1)<br><br>IXE total: -0,2 (1,6) |  |  |
|--|--|--|--|--|--|--|------------------|-------------------|--|--|--|--|

**mSASSS: % no progresores) (1 estudio)**

|  |                      |             |    |            |             |  |   |   |   |  |                       |            |
|--|----------------------|-------------|----|------------|-------------|--|---|---|---|--|-----------------------|------------|
| Van der Heijde<br>2022 (3)<br><br>(2 años) | Estudio de extensión | no es serio | NA | Es directa | No es serio |  | SPARCC columna >2 sem 52<br><br><u>Cambio mSASSS &lt;2</u><br><br>IXE/4s (n=21): 85,7%<br><br>IXE/2s (n=20): 80%<br><br>IXE total (n=41): 82,9% | SPARCC columna <2 sem 52<br><br><u>Cambio mSASSS &lt;2</u><br><br>IXE/4s (n=34): 97,1%<br><br>IXE/2s (n=34): 94,1%<br><br>IXE total (n=68): 95,6% | Según SPARCC sem 52<br><br><u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: RR 0,88 (0,73 – 1,06)<br><br>IXE/2s: RR 0,85 (0,67 – 1,07)<br><br>IXE total: RR 0,87 (0,75 – 1,01) | Según SPARCC sem 52<br><br><u>Cambio mSASSS &lt;2</u><br><br>IXE/4s: 113 menos por cada mil (de -258 a 60)<br><br>IXE/2s: 141 menos por cada mil (de -309 a 70)<br><br>IXE total: 127 menos por cada mil (de -241 a 6) | MODERADA <sup>a</sup> | importante |
|--|----------------------|-------------|----|------------|-------------|--|---|---|---|--|-----------------------|------------|

<sup>a</sup>Se considera evidencia moderada porque procede de estudio de extensión de calidad alta en donde, aunque ya no hay ciego por ser fase abierta, se mantienen los grupos de aleatorización.

<sup>b</sup>Estudios con muestras muy pequeñas y amplios intervalos de confianza en los resultados.

## Treatment optimisation

### Clinical question

In axSpA, can bDMARD therapy be tapered or withdrawn?

Pregunta: La suspensión del FAME biológico comparado con FAME biológico en administración a intervalo habitual para mantener la remisión en pacientes con espondiloartritis axial en remisión sostenida durante más de 6 meses

| Evaluación de certeza  |                    |                 |                |                     |             |                       | Nº de pacientes                  | Efecto  |                       | Certeza                                       | Importancia |         |
|--|--------------------|-----------------|----------------|---------------------|-------------|-----------------------|----------------------------------|---|-----------------------|---|-------------|---------|
| Nº de estudios   | Diseño de estudio  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | la suspensión del FAME biológico | FAME biológico en administración a intervalo habitual | Relativo (95% CI)     | Absoluto (95% CI)                             |             |         |
| <b>Mantener la remisión sin nuevos brotes (seguimiento: 10 meses)</b>    |                    |                 |                |                     |             |                       |                                  |   |                       |   |             |         |
| 1  | ensayos aleatorios | no es serio     | no es serio    | no es serio         | no es serio | ninguno               | 72/153 (47,1%)                   | 107/152 (70,4%)                                       | RR 0,66 (0,55 a 0,81) | 236 menos por 1000 (de 350 menos a 116 menos) | ⊕⊕⊕⊕ Alta   | CRÍTICO |
| <b>Mantener el estado de enfermedad inactiva (seguimiento: 10 meses)</b> |                    |                 |                |                     |             |                       |                                  |   |                       |   |             |         |
| 1  | ensayos aleatorios | no es serio     | no es serio    | no es serio         | no es serio | ninguno               | 51/153 (33,3%)                   | 87/152 (57,2%)  | RR 0,58 (0,45 a 0,76) | 241 menos por 1000 (de 337 menos a 131 menos) | ⊕⊕⊕⊕ Alta   | CRÍTICO |
| <b>Presentar brote (seguimiento: 10 meses)</b>                           |                    |                 |                |                     |             |                       |                                  |   |                       |   |             |         |
| 1  | ensayos aleatorios | no es serio     | no es serio    | no es serio         | no es serio | ninguno               | 81/153 (52,9%)                   | 45/152 (29,6%)  | RR 1,79 (1,34 a 2,38) | 233 más por 1000 (de 117 más a 347 más)       | ⊕⊕⊕⊕ Alta   | CRÍTICO |
| <b>Presentar un brote parcial (seguimiento: 10 meses)</b>                |                    |                 |                |                     |             |                       |                                  |   |                       |   |             |         |
| 1  | ensayos aleatorios | no es serio     | no es serio    | no es serio         | no es serio | Ninguno               | 98/153 (64,1%)                   | 62/152 (40,8%)  | RR 1,57 (1,25 a 1,97) | 232 más por 1000 (de 121 más a 331 más)       | ⊕⊕⊕⊕ Alta   | CRÍTICO |

Commentario: CI: Intervalo de confianza; RR: Razón de riesgos; ECA evaluado: Landewe R. Lancet. 2018;392(10142):134-44.

**Pregunta:** La interrupción del FAME biológico comparado con FAME biológico en administración a intervalo habitual para mantener la remisión en pacientes con espondiloartritis axial en remisión sostenida durante menos de 6 meses

| Evaluación de certeza   |                    |                    |                |                     |                    |                       | Nº de pacientes                  |   | Efecto                |   | Certeza          | Importancia |
|---|--------------------|--------------------|----------------|---------------------|--------------------|-----------------------|----------------------------------|---|-----------------------|---|------------------|-------------|
| Nº de estudios  | Diseño de estudio  | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | la suspensión del FAME biológico | FAME biológico en administración a intervalo habitual | Relativo (95% CI)     | Absoluto (95% CI)                             |                  |             |
| <b>Riesgo para mantener la remisión sin brote (seguimiento 10-12 meses)</b>                                 |                    |                    |                |                     |                    |                       |                                  |   |                       |   |                  |             |
| 3   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 71/219 (32,4%)                   | 185/221 (83,7%)                                       | RR 0,41 (0,23 a 0,72) | 494 menos por 1000 (de 645 menos a 234 menos) | ⊕⊕⊕○<br>Moderada | CRÍTICO     |
| <b>Riesgo para mantener la baja actividad (seguimiento 10-12 meses)</b>                                     |                    |                    |                |                     |                    |                       |                                  |   |                       |   |                  |             |
| 2   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 44/157 (28,0%)                   | 131/158 (82,9%)                                       | RR 0,36 (0,15 a 0,86) | 531 menos por 1000 (de 705 menos a 116 menos) | ⊕⊕⊕○<br>Moderada | CRÍTICO     |
| <b>Riesgo para mantener la enfermedad inactiva (seguimiento 10-12 meses)</b>                                |                    |                    |                |                     |                    |                       |                                  |   |                       |   |                  |             |
| 3   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 65/219 (29,7%)                   | 158/221 (71,5%)                                       | RR 0,40 (0,18 a 0,88) | 429 menos por 1000 (de 548 menos a 274 menos) | ⊕⊕⊕○<br>Moderada | CRÍTICO     |
| <b>Riesgo para mantener la remisión sin empeoramiento significativo del ASDAS (seguimiento 10-12 meses)</b> |                    |                    |                |                     |                    |                       |                                  |   |                       |   |                  |             |
| 1   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | serio <sup>b</sup> | ninguno               | 16/53 (30,2%)                    | 40/54 (74,1%)   | RR 0,41 (0,26 a 0,63) | 437 menos por 1000 (de 548 menos a 274 menos) | ⊕⊕○○<br>Baja     | CRÍTICO     |
| <b>Riesgo para presentar brote (seguimiento 10-12 meses)</b>  |                    |                    |                |                     |                    |                       |                                  |   |                       |   |                  |             |
| 1   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | serio <sup>b</sup> | ninguno               | 38/62 (61,3%)                    | 10/62 (16,1%)   | RR 3,86 (2,12 a 7,05) | 461 más por 1000 (de 181 más a 976 más)       | ⊕⊕○○<br>Baja     | CRÍTICO     |

**Comentarios:** Cl: Intervalo de confianza; MD: Diferencia media; RR: Razón de riesgo; ECAs evaluados: Landewe R. Ann Rheum Dis. 2020;79(7):920-8. Landewe R. Ann Rheum Dis. 2021;80(8):1022-30. Weinstein CLJ. Rheumatology (Oxford). 2023;62(11):3601-3609

a. Generación de la secuencia de aleatorización no clara.

b. Tamaño muestral bajo con una potencia estadística insuficiente.

Pregunta: El aumento de intervalo de FAME biológico comparado con FAME biológico en administración a intervalo habitual para mantener la remisión en pacientes con espondiloartritis axial en remisión sostenida durante más de 6 meses

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes                           |   | Efecto                   |                               | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|---|---|--------------------------|-------------------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | el aumento de intervalo de FAME biológico | FAME biológico en administración a intervalo habitual | Riesgo Relativo (95% CI) | Diferencia de Riesgo (95% CI) |         |             |

Riesgo de mantener en baja actividad de la enfermedad (según ASDAS)

|   |                    |             |             |             |                    |         |               |               |                       |                          |                  |         |
|---|--------------------|-------------|-------------|-------------|--------------------|---------|---------------|---------------|-----------------------|--------------------------|------------------|---------|
| 2 | ensayos aleatorios | No es serio | no es serio | no es serio | serio <sup>b</sup> | ninguno | 37/59 (62,7%) | 27/39 (69,2%) | RR 0,89 (0,66 a 1,18) | RD -6,5% (-25,5 a 12,5%) | ⊕⊕⊕○<br>Moderada | CRÍTICO |
|---|--------------------|-------------|-------------|-------------|--------------------|---------|---------------|---------------|-----------------------|--------------------------|------------------|---------|

Riesgo de mantener la enfermedad inactiva (según BASDAI) (seguimiento: 12 meses)

|   |                    |                    |             |             |                    |         |       |       |              |                    |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | -/55* | -/58* | no estimable | RD -6% (-21 a 10%) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|

Riesgo de mantener la enfermedad inactiva (según ASDAS)

|   |                    |                    |             |             |                    |         |       |       |              |                    |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | -/55* | -/58* | no estimable | RD -8% (-10 a 26%) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|

Riesgo de mantener en baja actividad de la enfermedad (según BASDAI)

|   |                    |                    |             |             |                    |         |       |       |              |                    |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | -/55* | -/58* | no estimable | RD -3% (-17 a 12%) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|

Riesgo de presentar nuevo brote (según ASDAS)

|   |                    |                    |             |             |                    |         |       |       |              |                    |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | -/55* | -/58* | no estimable | RD -6% (-25 a 13%) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|-------|-------|--------------|--------------------|--------------|---------|

Comentarios: CI: Intervalo de confianza; MD: Diferencia media; RR: Razón de riesgo. ECAs evaluado: Michielsens CAJ. Ann Rheum Dis. 2022 Oct;81(10):1392-1399. Ruwaard J. Scand J Rheumatol. 2023;52(2):129-136. Gratacós J. Arthritis Res Ther. 2019;21(1):11.

\*Los autores no proporcionan valores absolutos de este desenlace.

a. Riesgo de notificación selectiva no clara.

b. Tamaño muestral baja con una potencia estadística insuficiente.

Pregunta: El aumento de intervalo de administración del FAME biológico comparado con administración a intervalo habitual para mantener la remisión en pacientes con espondiloartritis axial en remisión sostenida durante menos de 6 meses

| Evaluación de certeza   |                    |                    |                |                     |                    |                       | Nº de pacientes  |                                     | Efecto                |  | Certeza       | Importancia |
|---|--------------------|--------------------|----------------|---------------------|--------------------|-----------------------|--|-------------------------------------|-----------------------|--|---------------|-------------|
| Nº de estudios  | Diseño de estudio  | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | el aumento de intervalo de administración del FAME biológico | administración a intervalo habitual | Relativo (95% CI)     | Absoluto (95% CI)                          |               |             |
| <b>Riesgo de mantener sin brotes</b>                              |                    |                    |                |                     |                    |                       |  |                                     |                       |  |               |             |
| 3   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 166/216 (76,9%)  | 185/221 (83,7%)                     | RR 0,93 (0,85 a 1,02) | 59 menos por 1000 (de 134 menos a 17 más)  | ⊕⊕⊕○ Moderada | CRÍTICO     |
| <b>Riesgo de mantener con baja actividad</b>                      |                    |                    |                |                     |                    |                       |  |                                     |                       |  |               |             |
| 2   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 117/153 (28,1%)  | 131/158 (35,4%)                     | RR 0,94 (0,81 a 1,09) | 50 menos por 1000 (de 158 menos a 75 más)  | ⊕⊕⊕○ Moderada | CRÍTICO     |
| <b>Riesgo de mantener la enfermedad inactiva</b>                  |                    |                    |                |                     |                    |                       |  |                                     |                       |  |               |             |
| 3   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | no es serio        | ninguno               | 140/216 (64,8%)  | 158/221 (71,5%)                     | RR 0,93 (0,76 a 1,14) | 50 más por 1000 (de 172 menos a 100 más)   | ⊕⊕⊕○ Moderada | CRÍTICO     |
| <b>Riesgo de mantener la remisión sin empeoramiento del ASDAS</b> |                    |                    |                |                     |                    |                       |  |                                     |                       |  |               |             |
| 1   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | serio <sup>b</sup> | ninguno               | 35/48 (72,9%)  | 40/54 (74,1%)                       | RR 0,98 (0,78 a 1,24) | 15 menos por 1000 (de 163 menos a 178 más) | ⊕⊕○○ Baja     | CRÍTICO     |
| <b>Riesgo de presentar un brote</b>                               |                    |                    |                |                     |                    |                       |  |                                     |                       |  |               |             |
| 1   | ensayos aleatorios | serio <sup>a</sup> | no es serio    | no es serio         | serio <sup>b</sup> | ninguno               | 15/63 (23,8%)  | 10/63 (15,9%)                       | RR 1,50 (0,73 a 3,08) | 79 más por 1000 (de 43 menos a 330 más)    | ⊕⊕○○ Baja     | CRÍTICO     |

Comentarios: CI: Intervalo de confianza; MD: Diferencia media; RR: Razón de riesgo; ECAs evaluados: Landewe R. Ann Rheum Dis. 2020;79(7):920-8. Landewe R. Ann Rheum Dis. 2021;80(8):1022-30. Weinstein CLJ.Rheumatology (Oxford).

2023;62(11):3601-3609

a. Generación de la secuencia de aleatorización no clara.

b. Tamaño muestral bajo con una potencia estadística insuficiente.

Pregunta: El aumento de intervalo de administración del FAME biológico comparado con la administración a intervalo habitual para mantener la remisión en pacientes con espondiloartritis axial en el momento de inclusión

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes  |                | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|--|----------------|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | el aumento de intervalo de administración del FAME biológico | dosis habitual | Relativo (95% CI) | Absoluto (95% CI) |         |             |

#### Riesgo de mantener la remisión

|   |                    |                    |             |             |                    |         |               |               |                       |  |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|---------------|---------------|-----------------------|--|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | 19/22 (86,4%) | 19/21 (90,5%) | RR 0,95 (0,77 a 1,18) | 45 menos por 1000 (de 208 menos a 163 más) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|---------------|---------------|-----------------------|--|--------------|---------|

#### Riesgo de presentar nuevo brote

|   |                    |                    |             |             |                    |         |              |             |                       |   |              |         |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|--------------|-------------|-----------------------|---|--------------|---------|
| 1 | ensayos aleatorios | serio <sup>a</sup> | no es serio | no es serio | serio <sup>b</sup> | ninguno | 3/22 (13,6%) | 2/21 (9,5%) | RR 1,43 (0,27 a 7,73) | 41 más por 1000 (de 70 menos a 641 más) | ⊕⊕○○<br>Baja | CRÍTICO |
|---|--------------------|--------------------|-------------|-------------|--------------------|---------|--------------|-------------|-----------------------|---|--------------|---------|

Comentarios: CI: Intervalo de confianza; RR: Razón de riesgo; ECA evaluado: Cantini F. Biologics. 2013;7:1-6.

a. Sin información sobre la generación de la secuencia de aleatorización. Riesgo de sesgo en medidas de desenlace y notificación selectiva de resultados no claro.

b. Tamaño muestral baja con una potencia estadística insuficiente.

## Extra-musculoskeletal manifestations

### Clinical question

In axSpA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)?

## 1. FAME BIOLÓGICOS

### 1.1. Comparación FAMEb versus placebo

**1.1.1. Enfermedad inflamatoria intestinal** (6 a 28 semanas): adalimumab, certolizumab, golimumab, etanercept, infliximab, secukinumab, ixekizumab y bimekizumab.

| Evaluación de certeza           |                   |                    |                    |                     |             |                       | Nº de pacientes |           | Efeto                                 |  | Certeza      | Importancia |
|---------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|-----------|---------------------------------------|--|--------------|-------------|
| Nº de estudios                  | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | FAMEb           | Placebo   | Cociente tasas de incidencia (95% CI) | Absoluto (95% CI)  |              |             |
| 1 RS <sup>(5)</sup><br>(22 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 5.6*/3845       | 3.4*/1895 | 1.6<br>(0.3 a 7.9)                    | 2.2 por 1000 pacientes por año<br>(de 4.1 menos a 8.5 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

ECA: ensayo clínico aleatorizado. FAMEb: fármacos modificadores de la enfermedad biológico. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. \* Tasa de incidencia de nuevos casos de EII por 1000 pacientes-año.

## 1.2. Comparación iTNF versus placebo

**1.2.1. Enfermedad inflamatoria intestinal:** número de **brotes** en pacientes con **EII conocida** (mediana de 16 semanas): adalimumab, certolizumab, golimumab, etanercept, infliximab.

| Evaluación de certeza           |                   |                    |                    |                     |             |                       | Nº de pacientes |               | Efecto                     |  | Certeza      | Importancia |
|---------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|---------------|----------------------------|--|--------------|-------------|
| Nº de estudios                  | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iTNF            | Placebo       | OR (95% CI)                | Absolute (95% CI)                          |              |             |
| 1 RS <sup>(6)</sup><br>(21 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 2/2559 (0.08%)  | 0/1697 (0.0%) | OR* 1.04<br>(0.09 a 11.40) | 0 menos por 1000<br>(de 0 menos a 0 menos) | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

**1.2.2. Enfermedad inflamatoria intestinal:** número de **nuevos brotes** en pacientes con **EII no conocida** (mediana de 16 semanas): adalimumab, certolizumab, golimumab, etanercept, infliximab.

|                                 |           |                    |                    |             |             |         |               |               |                           |  |              |         |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|---------------|---------------|---------------------------|--|--------------|---------|
| 1 RS <sup>(6)</sup><br>(21 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | No es serio | Ninguno | 4/2559 (0.2%) | 3/1697 (0.2%) | OR* 1.22<br>(0.27 a 5.48) | 0 menos por 1000<br>(de 1 menos a 8 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|---------------|---------------|---------------------------|--|--------------|---------|

ECA: ensayo clínico aleatorizado. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. El grupo de pacientes con espondiloartritis está integrado por espondilitis anquilosante, espondiloartritis axial no radiográfica y espondiloartritis periférica. \* *Odss ratio* por método de Peto.

## 1.3. Comparación iTNF monoclonal versus placebo

**1.3.1. Uveítis anterior** (media del periodo controlado, 22,7 semanas [DE 18,5]; mediana de 16 semanas [rango: 6–104]): adalimumab, certolizumab, golimumab, infliximab.

| Evaluación de certeza           |                   |                    |                |                     |             |                       | Nº de pacientes |                | Efecto                      |   | Certeza          | Importancia |
|---------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|----------------|-----------------------------|---|------------------|-------------|
| Nº de estudios                  | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | iTNF monoclonal | Placebo        | OR (95% CI)                 | Absolute (95% CI)                         |                  |             |
| 1 RS <sup>(7)</sup><br>(17 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 10/2101 (0.5%)  | 31/2497 (1.2%) | OR 4.990<br>(0.256 a 0.973) | 47 más por 1000<br>(de 9 menos a 0 menos) | ⊕⊕⊕⊖<br>Moderada | IMPORTANTE  |

ECA: ensayo clínico aleatorizado. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis. OR: *odd ratio*. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios.

## 1.4. Comparación Etanercept versus placebo

### 1.4.1. Enfermedad inflamatoria intestinal (6 a 28 semanas).

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes |           | Efecto                                |   | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|-----------|---------------------------------------|---|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | ETN             | Placebo   | Cociente tasas de incidencia (95% CI) | Absoluto (95% CI)   |              |             |
| 1 RS <sup>(5)</sup><br>(8 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 8.1*/856        | 3.4*/1895 | 2.4<br>(0.3 a 16.8)                   | 4.7 por 1000 pacientes por año<br>(de 7.5 menos a 16.9 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

ECA: ensayo clínico aleatorizado. ETN: etanercept. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. \* Tasa de incidencia de nuevos casos de EII por 1000 pacientes-año.

### 1.4.2. Uveítis anterior (media del periodo controlado, 22,7 semanas [DE 18,5]; mediana de 16 semanas [rango: 6–104]).

| Evaluación de certeza           |                   |                    |                |                     |             |                       | Nº de pacientes |                | Efecto                      |  | Certeza          | Importancia |
|---------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|----------------|-----------------------------|--|------------------|-------------|
| Nº de estudios                  | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | ETN             | Placebo        | OR (95% CI)                 | Absoluto (95% CI)                        |                  |             |
| 1 RS <sup>(7)</sup><br>(10 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 5/699 (0.7%)    | 31/2497 (1.2%) | OR 4.990<br>(0.198 a 1.259) | 47 más por 1000<br>(de 10 menos a 3 más) | ⊕⊕⊕⊖<br>Moderada | IMPORTANTE  |

ECA: ensayo clínico aleatorizado. ETN: etanercept. MA: metaanálisis. OR: *odd ratio*. RS: revisión sistemática.

<sup>a</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios.

## 1.5. Comparación Etanercept versus iTNF monoclonal

### 1.5.1. Enfermedad inflamatoria intestinal (12 a 28 semanas).

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes |                 | Efecto                                |  | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|-----------------|---------------------------------------|--|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | ETN             | iTNF monoclonal | Cociente tasas de incidencia (95% CI) | Absoluto (95% CI)  |              |             |
| 1 RS <sup>(5)</sup><br>(7 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 8.1*/856        | 2.4*/1105       | 3.5<br>(0.3 a 38.2)                   | 5.8 por 1000 pacientes por año (de 6.4 menos a 18.0 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

ETN. Etanercept. iTNF: inhibidores del factor de necrosis tumoral.

<sup>a</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. \* Tasa de incidencia de nuevos casos de EII por 1000 pacientes-año.

## 1.6. Comparación iIL-17 versus placebo

### 1.6.1. Enfermedad inflamatoria intestinal: número de brotes en pacientes con EII conocida (mediana de 16 semanas): secukinumab, ixekizumab.

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes |              | Efecto                     |                                      | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|--------------|----------------------------|--------------------------------------|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-17A         | Placebo      | OR (95% CI)                | Absoluto (95% CI)                    |              |             |
| 1 RS <sup>(6)</sup><br>(7 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 5/1177 (0.4%)   | 1/585 (0.2%) | OR* 2.12<br>(0.39 a 11.60) | 2 más por 1000 (de 1 menos a 18 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

### 1.6.2. Enfermedad inflamatoria intestinal: número de nuevos brotes en pacientes con EII no conocida (mediana de 16 semanas): secukinumab, ixekizumab.

|                                |           |                    |                    |             |             |         |                |              |                            |  |              |         |
|--------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|----------------------------|--|--------------|---------|
| 1 RS <sup>(6)</sup><br>(7 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | No es serio | Ninguno | 6/1177 (0.51%) | 0/585 (0.0%) | OR* 2.38<br>(0.49 a 11.40) | 0 menos por 1000<br>(de 0 menos a 0 menos) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|--------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|----------------------------|--|--------------|---------|

ECA: ensayo clínico aleatorizado. iIL-17: inhibidores de la interleucina 17. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. El grupo de pacientes con espondiloartritis está integrado por espondilitis anquilosante, espondiloartritis axial no radiográfica y espondiloartritis periférica. \* Odds ratio por el método de Peto.

### 1.6.3. Uveítis anterior (media del periodo controlado, 22,7 semanas [DE 18,5]; mediana de 16 semanas [rango: 6–104]): secukinumab, ixekinumab.

| Evaluación de certeza          |                   |                    |                |                     |             |                       | Nº de pacientes |                | Efecto                      |   | Certeza          | Importancia |
|--------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|----------------|-----------------------------|---|------------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-17A         | Placebo        | OR (95% CI)                 | Absolute (95% CI)                       |                  |             |
| 1 RS <sup>(7)</sup><br>(8 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 23/1744 (1.3%)  | 31/2497 (1.2%) | OR 1.345<br>(0.465 a 3.886) | 4 más por 1000<br>(de 7 menos a 34 más) | ⊕⊕⊖⊖<br>Moderada | IMPORTANTE  |

ECA: ensayo clínico aleatorizado. iIL17A: inhibidores de la interleucina 17A. MA: metaanálisis. OR: odds ratio. RS: revisión sistemática.

<sup>a</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios.

### 1.6.A. Brodalumab versus placebo

#### 1.6.A.1. Uveítis (16 semanas).

| Evaluación de certeza |                   |                    |                |                     |                    |                       | Nº de pacientes |             | Efecto      |                   | Certeza      | Importancia |
|-----------------------|-------------------|--------------------|----------------|---------------------|--------------------|-----------------------|-----------------|-------------|-------------|-------------------|--------------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | Brodalumab      | Placebo     | RR (95% CI) | Absolute (95% CI) |              |             |
| 1 ECA <sup>(11)</sup> | ECA               | Serio <sup>a</sup> | No es serio    | No es serio         | Serio <sup>b</sup> | Ninguno               | 0/80 (0.0%)     | 0/79 (0.0%) | NA          | NA                | ⊕⊕⊖⊖<br>Baja | IMPORTANTE  |

### 1.6.A.2. Enfermedad inflamatoria intestinal (16 semanas).

|                       |     |                    |             |             |                    |         |             |             |    |    |             |         |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|-------------|-------------|----|----|-------------|---------|
| 1 ECA <sup>(11)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 0/80 (0.0%) | 0/79 (0.0%) | NA | NA | ⊕⊕⊖<br>Baja | CRÍTICA |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|-------------|-------------|----|----|-------------|---------|

ECA: ensayo clínico aleatorizado. NA: no aplica. RR: riesgo relativo.

<sup>a</sup>Alto riesgo de sesgo porque esta medida de resultado no fue el objetivo primario del ECA, se recoge como posibles eventos adversos. <sup>b</sup>Pocos pacientes incluidos y corta duración del tratamiento controlado doble ciego para la detección de eventos adversos.

### 1.6.B. Bimekizumab versus placebo

#### 1.6.B.1. Enfermedad de Crohn (16 semanas).

| Evaluación de certeza |                   |                    |                |                     |                    |                       | Nº de pacientes |              | Efecto                    |  | Certeza     | Importancia |
|-----------------------|-------------------|--------------------|----------------|---------------------|--------------------|-----------------------|-----------------|--------------|---------------------------|--|-------------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | Bimekizumab     | Placebo      | RR (95% CI)               | Absoluto (95% CI)                          |             |             |
| 2 ECA <sup>(12)</sup> | ECA               | Serio <sup>a</sup> | No es serio    | No es serio         | Serio <sup>b</sup> | Ninguno               | 1/349 (0.3%)    | 0/237 (0.0%) | RR* 2.04<br>(0.08 a 4.87) | 0 menos por 1000<br>(de 0 menos a 0 menos) | ⊕⊕⊖<br>Baja | CRÍTICA     |

#### 1.6.B.2. Colitis ulcerosa (16 semanas).

|                       |     |                    |             |             |                    |         |              |              |                           |   |             |         |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|-------------|---------|
| 2 ECA <sup>(12)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 1/349 (0.3%) | 1/237 (0.4%) | RR 0.68<br>(0.04 a 10.80) | 1 menos por 1000<br>(de 4 menos a 41 más) | ⊕⊕⊖<br>Baja | CRÍTICA |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|-------------|---------|

#### 1.6.B.3. Uveítis (16 semanas).

|                       |     |                    |             |             |                    |         |              |               |                          |   |             |            |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|---------------|--------------------------|---|-------------|------------|
| 2 ECA <sup>(12)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 2/349 (0.6%) | 11/237 (4.6%) | RR 0.12<br>(0.03 a 0.55) | 41 menos por 1000<br>(de 45 menos a 21 menos) | ⊕⊕⊖<br>Baja | IMPORTANTE |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|---------------|--------------------------|---|-------------|------------|

ECA: ensayo clínico aleatorizado. RR: riesgo relativo.

<sup>a</sup>Alto riesgo de sesgo porque esta medida de resultado no fue el objetivo primario del ECA, se recoge como posibles eventos adversos. <sup>b</sup>Corta duración del tratamiento controlado doble ciego para la detección de eventos adversos. \* calculado por los revisores.

## 1.7. Comparación iIL-17A versus iTNF monoclonal

### 1.7.1. Enfermedad inflamatoria intestinal (12 a 28 semanas).

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes |                 | Efecto                                |   | Certeza | Importancia |         |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|-----------------|---------------------------------------|---|---------|-------------|---------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-17A         | iTNF monoclonal | Cociente tasas de incidencia (95% CI) | Absolute (95% CI)   |         |             |         |
| 1 RS <sup>(5)</sup><br>(7 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 7.0*/1884       | 2.4*/1105       | 3.0<br>(0.3 a 26.7)                   | 4.7 por 1000 pacientes por año<br>(de 3.6 menos a 13.0 más) | ⊕⊕⊖⊖    | Baja        | CRÍTICA |

ECA: ensayo clínico aleatorizado. iIL-17A: inhibidores de la interleucina 17A. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. \* Tasa de incidencia de nuevos casos de EII por 1000 pacientes-año.

## 2. FAME SINTÉTICOS DE DIANA ESPECÍFICA

### 2.1. Comparación iJAK versus placebo

#### 2.1.A. Upadacitinib versus placebo

##### 2.1.A.1. Enfermedad inflamatoria intestinal en pacientes con EspAax no radiográfica (14 semanas + 30 días).

| Evaluación de certeza |                   |                    |                |                     |                    |                       | Nº de pacientes |              | Efecto      |                   | Certeza      | Importancia |
|-----------------------|-------------------|--------------------|----------------|---------------------|--------------------|-----------------------|-----------------|--------------|-------------|-------------------|--------------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | Upadacitinib    | Placebo      | RR (95% CI) | Absoluto (95% CI) |              |             |
| 1 ECA <sup>(13)</sup> | ECA               | Serio <sup>a</sup> | No es serio    | No es serio         | Serio <sup>b</sup> | Ninguno               | 0/156 (0.0%)    | 0/157 (0.0%) | NA          | NA                | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

##### 2.1.A.2. Enfermedad inflamatoria intestinal en pacientes con espondilitis anquilosante (14 semanas + 30 días).

|                       |     |                    |             |             |                    |         |              |              |                           |   |              |         |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|--------------|---------|
| 1 ECA <sup>(14)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 0/211 (0.0%) | 1/209 (0.5%) | RR* 0.33<br>(0.01 a 8.06) | 3 menos por 1000<br>(de 5 menos a 34 más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|--------------|---------|

##### 2.1.A.3. Uveítis en pacientes con EspAax no radiográfica (14 semanas + 30 días).

|                       |     |                    |             |             |                    |         |              |              |                            |  |              |            |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----------------------------|--|--------------|------------|
| 1 ECA <sup>(13)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 1/156 (0.6%) | 0/157 (0.0%) | RR* 3.02<br>(0.12 a 73.55) | 0 menos por 1000<br>(de 0 menos a 0 menos) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----------------------------|--|--------------|------------|

##### 2.1.A.4. Uveítis en pacientes con espondilitis anquilosante (14 semanas + 30 días).

|                       |     |                    |             |             |                    |         |              |              |                           |   |              |            |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|--------------|------------|
| 1 ECA <sup>(14)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 1/211 (0.5%) | 3/209 (1.4%) | RR* 0.33<br>(0.03 a 3.15) | 10 menos por 1000<br>(de 14 menos a 31 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|---------------------------|---|--------------|------------|

#### 2.1.A.5. Psoriasis en pacientes con EspAax no radiográfica (14 semanas + 30 días).

|                       |     |                    |             |             |                    |         |              |              |    |    |              |            |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----|----|--------------|------------|
| 1 ECA <sup>(13)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 0/156 (0.0%) | 0/157 (0.0%) | NA | NA | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----|----|--------------|------------|

#### 2.1.A.6. Psoriasis en pacientes con espondilitis anquilosante (14 semanas + 30 días).

|                       |     |                    |             |             |                    |         |              |              |                            |   |              |            |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----------------------------|---|--------------|------------|
| 1 ECA <sup>(14)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 1/211 (0.5%) | 0/209 (0.0%) | RR* 2.97<br>(0.12 a 72.54) | 0 menos por 1000<br>(de 0 menos a 0<br>menos) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|----------------------------|---|--------------|------------|

ECA: ensayo clínico aleatorizado. RR\*: riesgo relativo calculado por los revisores.

<sup>a</sup> Alto riesgo de sesgo porque esta medida de resultado no fue el objetivo primario del ECA, se recoge como posibles eventos adversos. <sup>b</sup> Pocos pacientes y corta duración del tratamiento controlado doble ciego para la detección de eventos adversos.

#### 2.1.B. Tofacitinib versus placebo

##### 2.1.B.1. Enfermedad inflamatoria intestinal en pacientes con espondilitis anquilosante (16 semanas).

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |              | Efecto      |                   | Certeza      | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|--------------|-------------|-------------------|--------------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Tofacitinib     | Placebo      | RR (95% CI) | Absolute (95% CI) |              |             |
| 1 ECA <sup>(15)</sup> | ECA               | No es serio     | No es serio    | No es serio         | No es serio | Ninguno               | 0/133 (0.0%)    | 0/136 (0.0%) | NA          | NA                | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

##### 2.1.B.2. Uveítis en pacientes con espondilitis anquilosante (16 semanas).

|                       |     |                    |             |             |                    |         |              |              |                          |  |              |         |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|--------------------------|--|--------------|---------|
| 1 ECA <sup>(15)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 1/133 (0.8%) | 3/136 (2,2%) | RR 0.34<br>(0.04 a 3.24) | 15 menos por 1000<br>(de 21 menos a 49<br>más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|--------------------------|--|--------------|---------|

### 2.1.B.3. Psoriasis en pacientes con espondilitis anquilosante (16 semanas).

|                       |     |                    |             |             |                    |         |              |              |                                   |  |              |         |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|-----------------------------------|--|--------------|---------|
| 1 ECA <sup>(15)</sup> | ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 0/133 (0.0%) | 1/136 (0.7%) | <b>RR* 0.34<br/>(0.01 a 8.29)</b> | 5 menos por 1000<br>(de 7 menos a 54<br>más) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|-----------------------|-----|--------------------|-------------|-------------|--------------------|---------|--------------|--------------|-----------------------------------|--|--------------|---------|

ECA: ensayo clínico aleatorizado. RR\*: riesgo relativo calculado por los revisores.

<sup>a</sup>Alto riesgo de sesgo porque esta medida de resultado no fue el objetivo primario del ECA, se recoge como posibles eventos adversos. <sup>b</sup>Pocos pacientes y corta duración del tratamiento controlado doble ciego para la detección de eventos adversos.

## Obesity and smoking

### Clinical question

In axSpA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

Pregunta: No fumador vs. exfumador.

| Nº estudios   | Diseño de estudio                  | Evaluación de certeza |                |                     |   |  | Nº de pacientes           |                          | Efecto  |                   | Certeza          | Importancia |
|---------------|------------------------------------|-----------------------|----------------|---------------------|---|--|---------------------------|--------------------------|---|-------------------|------------------|-------------|
|               |                                    | Riesgo de sesgo       | Inconsistencia | Evidencia indirecta | Imprecisión   | Otras consideraciones  | No fumador                | Exfumador                | Relativo (IC 95%)   | Absoluto (IC 95%) |                  |             |
| <b>ASDAS</b>  |                                    |                       |                |                     |   |  |                           |                          |   |                   |                  |             |
| 2             | Estudio observacional <sup>1</sup> | No serio              | NA             | No serio            | Serio<br>N pequeña para mujeres fumadoras y exfumadoras | falta información acerca del tiempo de cese del hábito tabáquico y la duración e intensidad    | Hombres 89<br>Mujeres 105 | Hombres 36<br>Mujeres 42 | <b>ASDAS- PCR a 1 año (referencia no fumadores):</b><br>- Todos: $\beta 0,18$ (IC 95% 0,03 a 0,39)<br>- Hombres: $\beta 0,01$ (IC 95% 0,30 a 0,31)<br>- Mujeres: $\beta 0,38$ (IC 95% 0,09 a 0,67); $p < 0,05$                            |                   | ⊕○○○<br>Muy baja | CRÍTICA     |
|               | Estudio observacional <sup>2</sup> | No serio              | NA             | No serio            | No serio  |  | 234                       | 187                      | <b>ASDAS basal</b><br>No fumadores 2,9 (2,4 a 3,4)<br>Exfumadores 3,0 (2,4 a 3,5)<br>$p = 0,042$<br><br><b>Reducción ASDAS a los:</b><br>- 3m: $\beta -0,07$ (IC 95% -0,47 a 0,32)<br>- 6m: $\beta 0,02$ (IC 95% -0,10 a 0,13)            |                   | ⊕⊕○○<br>Baja     | CRÍTICA     |
| <b>BASDAI</b> |                                    |                       |                |                     |   |  |                           |                          |   |                   |                  |             |
| 2             | Estudio observacional <sup>1</sup> | No serio              | NA             | No serio            | Serio<br>N pequeña para mujeres fumadoras y exfumadoras | falta información acerca del tiempo de cese del hábito tabáquico y la duración e intensidad NA | Hombres 89<br>Mujeres 105 | Hombres 36<br>Mujeres 42 | <b>BASDAI Q2 (dolor axial)</b><br>- Hombres: $\beta -0,40$ (IC 95% -1,24 a 0,43)<br>- Mujeres: $\beta 0,19$ (IC 95% -0,65 a 1,02)<br><br><b>BASDAI Q6 (duración de rigidez matutina)</b><br>- Hombres: $\beta 0,06$ (IC 95% -0,83 a 0,95) |                   | ⊕○○○<br>Muy baja | IMPORTANTE  |

|   |                                    |          |    |          |          |  |     |   |   |              |            |
|---|------------------------------------|----------|----|----------|----------|--|-----|---|---|--------------|------------|
|   |                                    |          |    |          |          |  |     | - Mujeres: $\beta$ 1,09 (IC 95% 0,16 – 2,02)<br>$P <0,05$ |   |              |            |
|   | Estudio observacional <sup>2</sup> | No serio | NA | No serio | No serio |  | 234 | 187   | <b>BASDAI basal</b><br>No fumadores 6,4 (5,1 a 7,4)<br>Exfumadores 6,8 (5,5 a 8,1)<br>$p= 0,004$<br><br><b>BASDAI a los:</b><br>- 3m: $\beta$ -0,58 (IC 95% -1,41 a 0,25)<br>- 6m: $\beta$ 0,07 (IC 95% -0,11 a 0,24) | ⊕⊕○○<br>Baja | IMPORTANTE |
| <b>BASFI</b>                              |                                    |          |    |          |          |  |     |   |   |              |            |
| 1   | Estudio observacional <sup>2</sup> | No serio | NA | No serio | No serio |  | 234 | 187   | <b>BASFI media basal</b><br>No fumadores 6,0 (4,1 a 7,7)<br>Exfumadores 6,7 (5,0 a 8,3)<br>$p<0,001$<br><br><b>BASFI a los:</b><br>- 3m: $\beta$ -0,59 (-1,40 a 0,22)<br>- 6m: 0,03 (-0,18 a 0,23)                    | ⊕⊕○○<br>Baja | IMPORTANTE |
| <b>Supervivencia del fármaco anti-TNF</b> |                                    |          |    |          |          |  |     |   |   |              |            |
| 1   | Estudio observacional <sup>3</sup> | No serio | NA | No serio | No serio |  | 224 | 177   | <b>HR</b><br>- Todas las causas 0,68 (IC 95% 0,45 a 1,04)<br>- Infecciones 1,03 (IC 95% 0,55 a 1,96)<br>- Otros eventos adversos 1,02 (IC 95% 0,50 a 2,07)<br>- Ineficacia 0,73 (0,39 a 1,37)                         | ⊕⊕○○<br>Baja | IMPORTANTE |

Referencias: 1. Exarchou, 2022. 2. Zhao, 2020. 3. Zhao, 2019.

Notas:

\*El coeficiente  $\beta$  se interpreta al igual que se hace con una diferencia de medias. Es decir, muestra la diferencia del valor medio extraído del modelo.

\*\* ASDAS-MI: Major Improvement in the Ankylosing Spondylitis Disease Activity Score

## Pregunta: No fumador vs. Fumador

| Nº estudios   | Diseño de estudio  | Evaluación de certeza |                    |                     |             |   |                             | Nº de pacientes            |  | Efecto  |                   | Certeza    | Importancia |
|---------------|--|-----------------------|--------------------|---------------------|-------------|---|-----------------------------|----------------------------|--|---|-------------------|------------|-------------|
|               |  | Riesgo de sesgo       | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones   |                             | No fumador                 | Fumador  | Relativo (IC 95%)   | Absoluto (IC 95%) |            |             |
| <b>ASDAS</b>  |  |                       |                    |                     |             |   |                             |                            |  |   |                   |            |             |
| 3             | RS <sup>1</sup><br>(estudio observacional) <sup>2</sup>          | No serio              | NA                 | No serio            | Serio       |   | ND                          | ND                         | Remisión por ASDAS <1,3<br>- Basal: OR = 0,22 (0,08-0,56)<br>- A los 2 años: OR = 0,34 (0,13-0,87) |   | ⊕○○○<br>Muy baja  | CRÍTICA    |             |
|               | Estudio observacional <sup>3</sup>                               | No serio              | NA                 | No serio            | Serio       | Falta información acerca del tiempo de cese del hábito tabáquico y la duración e intensidad.  | Hombres: 89<br>Mujeres: 105 | Hombres: 35<br>Mujeres: 17 |  | ASDAS- PCR a 1 año (referencia no fumadores):<br>- Todos: β 0,24 (IC 95% -0,03 a 0,50)<br>- Hombres: β 0,15 (IC 95% -0,22 a 0,52)<br>- Mujeres: β 0,28 (IC 95% -0,12 a 0,67)                            | ⊕○○○<br>Muy baja  | CRÍTICA    |             |
|               | Estudio observacional <sup>4</sup>                               | No serio              | NA                 | No serio            | No serio    |   | 234                         | 206                        |  | ASDAS Basal<br>No fumadores 2,9 (IC 95% 2,4 a 3,4)<br>Fumadores 3,0 (IC 95% 2,6 a 3,6); p=0,042<br><br>ASDAS a los:<br>- 3m: β -0,01 (IC 95% -0,42 a 0,40); - 6m: β 0,10 (IC 95% 0,002 a 0,20) p < 0,05 | ⊕⊕○○<br>Baja      | CRÍTICA    |             |
| <b>BASDAI</b> |  |                       |                    |                     |             |   |                             |                            |  |   |                   |            |             |
| 4             | RS <sup>5</sup><br>(8 estudios observacionales <sup>6-13</sup> ) | Serio <sup>a</sup>    | Serio <sup>b</sup> | Son serio           | No serio    | La mayoría de los estudios eran transversales con baja calidad. Además, una alta heterogeneidad en cuanto a diseño, evaluación de tabaquismo y población. | 40                          | 35                         | OR: 2,905 (IC 95% 0,922 a 9,155); p=0,069  | BASDAI (DE)<br>No fumadores: 3,84 (2,11)<br>Fumadores: 4,30 (1,91) (p=0,283)<br><br>β =0,05 (IC 95% 0-0,094; p=0,05)  | ⊕○○○<br>Muy baja  | IMPORTANTE |             |
|               |  |                       |                    |                     |             |   | 113                         | 47                         |  |   |                   |            |             |

|   |          |    |          |                 |                                    |             |  |   |   |            |  |
|---|----------|----|----------|-----------------|------------------------------------|-------------|--|---|---|------------|--|
|   |          |    |          |                 | 104                                | 22          |  | $\beta = 1,39$ (IC 95% 0,52-2,26;<br>$p=0,002$ )  |   |            |  |
|   |          |    |          |                 | 24                                 | 24          | <b>OR: 1,83 (IC 95% 1,13-2,98) p=0,015</b> | BASDAI (media) fumadores<br>$33,87 \pm 11,71$ vs no fumadores<br>$19,54 \pm 10,95$<br><b>P= 0,000</b>                   |   |            |  |
|   |          |    |          |                 | 308                                | 127         | <b>OR=1,62 (IC 95% 1,03- 2,55; p=0,04)</b> | BASDAI<br>- No fumadores: 4,0 (2,0-6,0)<br>- Fumadores: 5,0 (3,0-7,0)<br>$p=0,10$                                       |   |            |  |
|   |          |    |          |                 | 185                                | 56          |  | $\beta = 14,75$ IC 95% 7,0, 22,49; <b>p &lt;0,001</b>   |   |            |  |
|   |          |    |          |                 | 50                                 | 56          |  | <b>BASDAI</b><br>- No fumadores: $3,2 \pm 1,5$<br>- Fumadores: $4,8 \pm 2,3$<br>$p<0,001$<br>$\beta = 0,35$ ; $p<0,001$ |   |            |  |
|   |          |    |          |                 | 174                                | 123         |  | <b>BASDAI:</b><br>- No fumadores: $4,3 \pm 2,1$<br>- Fumadores: $4,6 \pm 1,9$<br>$p=0,06$                               |   |            |  |
|   |          |    |          |                 |                                    |             |  | <b><math>\beta 0,50</math>,</b><br>(IC 95% 0,17-<br>0,83; <b>p=0,003</b> )  |   |            |  |
| RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio | NA | No serio | Serio           | No se identifica la n de pacientes | ND          | ND   | Remisión por BASDAI < 3,6<br>- Basal: OR = 0,39 (0,16-0,95)<br>- A los 2 años: OR = 0,31 (0,15-0,63)                    | ⊕○○○<br>Muy baja  | IMPORTANTE |  |
| Estudio observacional <sup>3</sup>                    | No serio | NA | No serio | Serio N pequeña |                                    | Hombres 89  | Hombres 35                                 |   | <b>BASDAI Q2 (dolor axial)</b><br>- Hombres: $\beta 0,58$ (IC 95% – 1(-0,43 a 1,59)<br>- Mujeres: $\beta 1,36$ (IC 95% – (0,19–2,53)<br><b>P &lt;0,05</b> |            |  |
|   |          |    |          |                 |                                    | Mujeres 105 | Mujeres 17                                 |   |   |            |  |

|              |   |       |       |          |       |   |   |  |  |  |              |            |
|--------------|---|-------|-------|----------|-------|---|---|--|--|--|--------------|------------|
|              |   |       |       |          |       |   |   | <b>BASDAI Q3</b> (síntomas articulares periféricos)<br>- <b>Hombres:</b> $\beta$ -0,47 (IC 95% – 1,49 a 0,55)<br>- <b>Mujeres:</b> $\beta$ 0,86 (IC 95% – 0,40 a 2,12) |  |  |              |            |
|              |   |       |       |          |       |   |   | <b>BASDAI Q6</b> (duración de rigidez matutina)<br>- <b>Hombres:</b> $\beta$ 0,58 (IC 95% (-0,50 a 1,65)<br>- <b>Mujeres:</b> $\beta$ 1,22 (IC 95% – 0,07 a 2,50)      |  |  |              |            |
| <b>BASFI</b> |   |       |       |          |       |   |   |  |  |  |              |            |
| 2            | RS <sup>5</sup> (7 estudios observacionales <sup>6,13</sup> ) | Serio | Serio | No serio | Serio | La mayoría de los estudios eran transversales con baja calidad. Además, una alta heterogeneidad en cuanto a diseño, evaluación de tabaquismo y población. | 40<br>-----<br>104<br>-----<br>24<br>-----<br>308<br>-----<br>191<br>-----<br>185<br>-----<br>174 | 35<br>-----<br>22<br>-----<br>24<br>-----<br>127<br>-----<br>120<br>-----<br>56<br>-----<br>123  | BASFI ( $\geq 1,5$ vs. <1,5)<br><b>OR</b> 1,661 (IC 95% 0,622 a 4,431);<br>$p=0,311$<br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><b>OR</b> 1,39 (1,15–1,68)<br>$p=0,0007$ | Media (DE)<br>No fumador: 2,05 (2,16)<br>Fumador: 2,54 (2,30)<br>$p=0,240$<br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><b>BASFI media +DE</b><br><b>Fumadores:</b> $40,04 \pm 18,55$<br><b>No fumadores:</b> $22,75 \pm 16,40$<br>$p=0,002$<br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><b>BASFI</b><br>- No fumadores: 4,0 (2,0–6,0)<br>- Fumadores: 5,0 (3,0–8,0) $p<0,0001$ | ⊕⊕○○<br>Baja | IMPORTANTE |

|               |  |          |          |          |          |                                    |                                    |                                   |  |  |                  |            |
|---------------|--|----------|----------|----------|----------|------------------------------------|------------------------------------|-----------------------------------|--|--|------------------|------------|
|               |  |          |          |          |          |                                    |                                    |                                   |  | Regresión multivariable:<br>0,618 (0,0108–1,22) p=0,02<br>-----<br><b>BASFI</b><br>- No fumadores: 4,2 ± 2,3<br>- Fumadores: 5,3 ± 2,8<br>p=0,059<br><br>B= 0,06 p=0,307<br>-----<br><b>BASFI</b><br>- No fumadores: 2,8±2,3<br>- Fumadores: 3,4±2,2<br>p=0,001<br><br>β = 0,38 (IC 95% 0,07 a 0,69);<br>p=0,02  |                  |            |
|               | Estudio observacional <sup>4</sup>                             | No serio | NA       | No serio | No serio |                                    | 234                                | 162                               |  | <b>BASFI media basal</b><br>No fumadores: 6,0 (4,1 a 7,7)<br>Fumadores: 7,1 (5,5 a 8,5)<br>p<0,001<br><br><b>BASFI a los:</b><br>- 3m: β 0,21 (-0,61 a 1,03)<br>- 6m: β 0,02 (-0,19 a 0,23)  | ⊕⊕○○<br>Baja     | IMPORTANTE |
| <b>mSASSS</b> |  |          |          |          |          |                                    |                                    |                                   |  |  |                  |            |
| 4             | RS <sup>5</sup> (estudio observacional <sup>14, 12, 13</sup> ) | Serio    | No serio | Serio    | Serio    | Ajustan por factores de confusión. | 49<br>-----<br>185<br>-----<br>174 | 48<br>-----<br>56<br>-----<br>123 |  | Incremento de mSASSS a los 2 años por cada unidad incrementada de ASDAS (IC 95%).<br><br>- <b>Todos</b> : fumadores 1,94 (1,00 a 2,87) vs no fumadores 0,35 (0,04 a 0,65); <b>p&lt;0,001</b><br><br>- <b>Hombres</b> : fumadores 2,15 (1,01 a 3,30) vs no fumadores 0,44 (0,02 a 0,86); <b>p&lt;0,001</b><br><br>- <b>Mujeres</b> : fumadoras 0,47 (-0,12 a 1,06) vs no fumadoras 0,16 (-0,13 a 0,44); <b>p&lt;0,001</b> | ⊕○○○<br>Muy baja | CRÍTICA    |

|   |  |          |          |          |          |   |                     |  |  |  |              |            |
|---|--|----------|----------|----------|----------|---|---------------------|--|--|--|--------------|------------|
|   |  |          |          |          |          |   |                     | <b>espalda:</b> OR 2,02,<br>$p=0,01$ ) | <b><math>\beta</math> 0,25; <math>p=0,001</math></b><br>-----<br><b><math>\beta</math> 0,54 (0,05 a 1,03); <math>p=0,03</math></b>   |  |              |            |
|   | RS <sup>1</sup> (estudio observacional <sup>15, 16)</sup>      | No serio | No serio | No serio | No serio |   | 149<br>-----<br>147 | 17<br>-----<br>63                      | <b>Progresión de <math>\geq 2</math> unidades mSASSS a los 5 años:</b><br>- <b>Todos:</b> OR = 1,44 (0,50-4,14), $p=0,50$<br>- <b>Hombres:</b> OR = 3,33 (0,74-15,00), $p=0,12$<br>- <b>Mujeres:</b> OR = 0,48 (0,06-4,18), $p=0,51$<br><br><b>Progresión de <math>\geq 2</math> unidades mSASSS a los 2 años:</b><br>OR = 2,75 (1,25-6,05), $p=0,012$ |  | ⊕⊕○○<br>Baja | CRÍTICA    |
|   | RS <sup>17</sup> (estudio observacional <sup>14, 12, 13)</sup> | No serio | No serio | No serio | No serio | Solo se incluyeron estudios transversales | 556                 | 643                                    | <b>Resultado del metaanálisis:</b><br><b>Presencia de sindesmofitos: OR: 2,02 con 95% IC (1,51–2,70).</b><br>Heterogeneidad entre estudios: $I^2=23,0\%$ , $p=0,25$  |  | ⊕⊕○○<br>Baja | CRÍTICA    |
|   | Estudio observacional <sup>18</sup>                            | No serio | No serio | NA       | No serio |   | 244                 | 162                                    | Inflamación en columna por RMN: <b><math>\beta = 1,69</math></b> [IC 95% 0,45-2,93)]; $P < 0,05$<br><br>Daño estructural en SI por RMN: <b><math>\beta = 0,57</math></b> (IC 95% 0,18,-0,96)]; $P < 0,05$<br><br>mSASSS score: <b><math>\beta = 0,26</math></b> (IC 95% -0,35- 0,86)   |  | ⊕⊕○○<br>Baja | CRÍTICA    |
| <b>Supervivencia del fármaco anti-TNF</b> |  |          |          |          |          |   |                     |  |  |  |              |            |
| 1   | Estudio observacional <sup>19</sup>                            | No serio | NA       | No serio | No serio |   | 224                 | 197                                    | <b>HR</b><br>- <b>Todas las causas</b> 0,79 (IC 95% 0,53 a 1,20)<br>- <b>Infecciones</b> 0,79 (IC 95% 0,40 a 1,54)<br>- <b>Otros eventos adversos</b> 0,86 (IC 95% 0,41 a 1,78)  |  | ⊕⊕○○<br>Baja | IMPORTANTE |

|  |  |  |  |  |  |  |  |  |   |  |  |  |
|--|--|--|--|--|--|--|--|--|---|--|--|--|
|  |  |  |  |  |  |  |  |  | - Ineficacia 1,44 (IC<br>95% 0,86 a 2,41) |  |  |  |
|--|--|--|--|--|--|--|--|--|---|--|--|--|

Referencias: 1. Wieczorek, 2021. 2. Wendling, 2017. 3. Exarchou, 2022. 4. Zhao, 2020. 5. Villaverde-García, 2016. 6. Chen, 2013. 7. Fallahi, 2013. 8. Reed, 2008. 9. Kaan, 2005. 10. Mattey, 2011. 11. Zhang, 2015. 12. Sakellariou, 2015. 13. Chung, 2012. 14. Ramiro 2015. 15. Deminger, 2018. 16. Poddubnyy, 2012. 17. Akar, 2017. 18. Nikiphorou, 2020. 19. Zhao, 2019.

Notas:

Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.

\*El coeficiente  $\beta$  se interpreta al igual que se hace con una diferencia de medias. Es decir, muestra la diferencia del valor medio extraído del modelo

Pregunta: Sobrepeso vs. normopeso.

| Nº estudios    | Diseño de estudio                                     | Riesgo de sesgo    | Inconsistencia | Evaluación de certeza |             |   | Sobrepeso | Normopeso | Efecto   |                   | Certeza      | Importancia |
|----------------|---|--------------------|----------------|-----------------------|-------------|---|-----------|-----------|--|-------------------|--------------|-------------|
|                |   |                    |                | Evidencia indirecta   | Imprecisión | Otras consideraciones   |           |           | Relativo (IC 95%)  | Absoluto (IC 95%) |              |             |
| <b>ASAS 40</b> |   |                    |                |                       |             |   |           |           |  |                   |              |             |
| 1              | RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio           | NA             | No serio              | No serio    | Ajustan por factores de confusión.  | ND        | ND        | OR 0,62 (IC 95% 0,24 a 1,14)   |                   | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>ASDAS</b>   |   |                    |                |                       |             |   |           |           |  |                   |              |             |
| 1              | Estudio observacional <sup>3</sup>                    | Serio <sup>a</sup> | NA             | Serio <sup>b</sup>    | No serio    | Hay datos perdidos para ASDAS.<br>No especifican cómo calculan el ASDAS, si con PCR o VSG.<br>Población asiática. | ND        | ND        | <b>ASDAS basal: <math>\beta 0,14</math></b><br>(IC 95% -0,03 a 0,30; p=0,106)<br><br><b>Δ ASDAS:</b><br>- 3m: $\beta 0,39$<br>(IC 95% 0,02 a 0,76; p=0,04)<br>- 6m: $\beta 0,52$<br>(IC 95% 0,13 a 0,91; p=0,01)<br>- 9m: $\beta 0,58$<br>(IC 95% 0,07 a 1,09; p=0,026)<br>- 12m: $\beta 0,38$<br>(IC 95% -0,07 a 0,93; p=0,077) | ⊕○○○<br>Muy baja  | CRÍTICA      |             |

| Nº estudios   | Diseño de estudio   | Riesgo de sesgo      | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones   | Evaluación de certeza   |  | Nº de pacientes   |  | Efecto  |                  | Certeza     | Importancia |
|---------------|---|----------------------|----------------|---------------------|-------------|---|---|--|-------------------|--|---|------------------|-------------|-------------|
|               |   |                      |                |                     |             |   | Sobrepeso   | Normopeso  | Relativo (IC 95%) | Absoluto (IC 95%)                      |   |                  |             |             |
| <b>BASDAI</b> |   |                      |                |                     |             |   |   |  |                   |  |   |                  |             |             |
| 2             | RS <sup>4</sup> (6 estudios observacionales) <sup>5,10)</sup><br><br>Estudio observacional <sup>3</sup> | Serio <sup>c,a</sup> | No serio       | No serio            | No serio    | En la RS, los estudios incluidos no ajustan por factores de confusión.<br><br>Población asiática. | 578<br>-----<br>- 3m: 64<br>- 6m: 51<br>- 9m: 37<br>- 12m: 43 | 748<br>-----<br>- 3m: 117<br>- 6m: 82<br>- 9m: 49<br>- 12m: 71 |                   |  | Diferencia de medias -0,09 (IC 95% -0,33 a 0,15)<br><br>BASDAI basal: β 0,10 (IC 95% -0,17 a 0,37; p=0,485)<br><br>Δ BASDAI:<br>- 3m: β 0,58 (IC 95% 0,13 a 1,02; p=0,011)<br>- 6m: β 0,69 (IC 95% 0,14 a 1,23; p=0,014)<br>- 9m: β 0,76 (IC 95% 0,07 a 1,45; p=0,031)<br>- 12m: β 1,20 (IC 95% 0,24 a 1,76; p=0,028) | ⊕○○○<br>Muy baja | IMPORTANT E |             |
| <b>BASFI</b>  |   |                      |                |                     |             |   |   |  |                   |  |   |                  |             |             |
| 1             | Estudio observacional <sup>3</sup>  | Serio <sup>a</sup>   | NA             | Serio <sup>b</sup>  | No serio    | Población asiática.   | ND  | ND   |                   | β -0,05 (IC 95% -0,31 a 0,22; p=0,728) | ⊕○○○<br>Muy baja  | IMPORTANT E      |             |             |

| Evaluación de certeza            |   |                 |                |                     |             |                                    | Nº de pacientes |           | Efecto                               |                   | Certeza      | Importancia |  |  |
|----------------------------------|---|-----------------|----------------|---------------------|-------------|------------------------------------|-----------------|-----------|--------------------------------------|-------------------|--------------|-------------|--|--|
| Nº estudios                      | Diseño de estudio                                     | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones              | Sobrepeso       | Normopeso | Relativo (IC 95%)                    | Absoluto (IC 95%) |              |             |  |  |
| <b>Supervivencia del fármaco</b> |   |                 |                |                     |             |                                    |                 |           |                                      |                   |              |             |  |  |
| <b>Anti-TNF</b>                  |   |                 |                |                     |             |                                    |                 |           |                                      |                   |              |             |  |  |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio        | NA             | No serio            | No serio    | Ajustan por factores de confusión. | ND              | ND        | HR 0,98 (IC 95% 0,79 a 1,38; p=0,92) |                   | ⊕⊕○○<br>Baja | IMPORTANT E |  |  |

Referencias: 1. Gialouri 2023. 2. Micheroli 2017. 3. Lidong 2021. 4. Ortolan 2021. 5. Al-Osami 2018. 6. Lee 2017. 7. Maas 2016. 8. Micheroli 2017. 9. Ottaviani 2012. 10. Rosas 2017.

Notas:

- a. Puntuación obtenida mediante la Escala de Newcastle Ottawa de 6 puntos (alto riesgo de sesgo).
  - b. Población asiática, con categorías de IMC diferentes: IMC bajo (<18,5); IMC normal (18,5-24); sobrepeso (IMC 24- 28); y obesidad (IMC >28).
  - c. Evaluación del riesgo de sesgo de la RS mediante herramienta ROBIS con resultado poco claro. Incluyen estudios con gran heterogeneidad clínica, analizando de forma conjunta aquellos de diseño transversal y observacionales, sin que realicen la mayoría de los estudios ajuste de resultados por posibles factores de confusión.
- \*El coeficiente  $\beta$  se interpreta al igual que se hace con una diferencia de medias. Es decir, muestra la diferencia del valor medio extraído del modelo.

Pregunta: Obesidad vs. normopeso

| Evaluación de certeza |   |                      |                |                     |             |   | Nº de pacientes |           | Efecto   |                   | Certeza      | Importancia |
|-----------------------|---|----------------------|----------------|---------------------|-------------|---|-----------------|-----------|--|-------------------|--------------|-------------|
| Nº estudios           | Diseño de estudio   | Riesgo de sesgo      | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones   | Obesidad        | Normopeso | Relativo (IC 95%)  | Absoluto (IC 95%) |              |             |
| <b>ASAS 40</b>        |   |                      |                |                     |             |   |                 |           |  |                   |              |             |
| 1                     | RS <sup>1</sup> (estudio observacional <sup>2</sup> )   | No serio             | NA             | No serio            | No serio    | Ajustan por factores de confusión.  | ND              | ND        | OR 0,27 (IC 95% 0,09 a 0,70)   |                   | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>ASDAS</b>          |   |                      |                |                     |             |   |                 |           |  |                   |              |             |
| 1                     | Estudio observacional <sup>3</sup><br><br>RS <sup>1</sup> (estudio observacional <sup>4</sup> ) | Serio <sup>a,b</sup> | No serio       | Serio <sup>c</sup>  | No serio    | Hay datos perdidos para ASDAS.<br>No especifican cómo calculan el ASDAS, si con PCR o VSG.<br>Población asiática.<br>-----<br>No ajustan por factores de confusión. | ND              | ND        | <b>ASDAS basal:</b><br>$\beta 0,36$<br>(IC 95% 0,15 a 0,57; p=0,001)<br><b>Δ ASDAS:</b><br>- 3m: $\beta 0,56$<br>(IC 95% 0,06 a 1,07; p=0,029)<br>- 6m: $\beta 0,79$<br>(IC 95% 0,29 a 1,28; p=0,002)<br>- 9m: $\beta 0,63$<br>(IC 95% 0,003 a 1,33; p=0,048)<br>- 12m: $\beta 0,69$<br>(IC 95% 0,05 a 1,32; p=0,034)<br>-----<br><b>ASDAS-VSG media (DE):</b><br>Obesos 2,58 (0,79)<br>Normopeso 1,9 (0,83)<br>p=0,03 | ⊕○○○<br>Muy baja  | CRÍTICA      |             |

| Nº estudios   | Diseño de estudio  | Riesgo de sesgo      | Evaluación de certeza |                     |             |   | Nº de pacientes   |  | Efecto            |   | Certeza          | Importancia |
|---------------|--|----------------------|-----------------------|---------------------|-------------|---|---|--|-------------------|---|------------------|-------------|
|               |  |                      | Inconsistencia        | Evidencia indirecta | Imprecisión | Otras consideraciones   | Obesidad  | Normopeso  | Relativo (IC 95%) | Absoluto (IC 95%)   |                  |             |
| <b>BASDAI</b> |  |                      |                       |                     |             |   |   |  |                   |   |                  |             |
| 2             | RS <sup>5</sup> (6 estudios observacional es <sup>6,11</sup> )<br><br>Estudio observacional <sup>3</sup> | Serio <sup>d,a</sup> | No serio              | No serio            | No serio    | En la RS, los estudios incluidos no ajustan por factores de confusión.<br><br>Población asiática. | 335<br>-----<br>- 3m: 25<br>- 6m: 24<br>- 9m: 14<br>- 12m: 22 | 748<br>-----<br>- 3m: 117<br>- 6m: 82<br>- 9m: 49<br>- 12m: 71 |                   | Diferencia de medias -0,78 (IC 95% -1,07 a -0,48)<br><br>- BASDAI basal: $\beta$ 0,63 (IC 95% 0,26 a 1,01; p=0,001)<br><br>Δ BASDAI:<br>- 3m: $\beta$ 0,80 (IC 95% 0,16 a 1,43; p=0,014)<br>- 6m: $\beta$ 0,92 (IC 95% 0,21 a 1,62; p=0,011)<br>- 9m: $\beta$ 1,21 (IC 95% 0,18 a 2,24; p=0,021)<br>- 12m: $\beta$ 1,30 (IC 95% 0,14 a 2,05; p=0,019) | ⊕○○○<br>Muy baja | IMPORTANTE  |
| <b>BASFI</b>  |  |                      |                       |                     |             |   |   |  |                   |   |                  |             |
| 1             | Estudio observacional <sup>3</sup>   | Serio <sup>a</sup>   | NA                    | Serio <sup>c</sup>  | No serio    | Población asiática.   | ND  | ND   |                   | $\beta$ 0,59 (IC 95% 0,22 a 0,96; p=0,002)  | ⊕○○○<br>Muy baja | IMPORTANTE  |

| Evaluación de certeza            |   |                 |                |                     |             |                                    | Nº de pacientes |           | Efecto   |                   | Certeza      | Importancia |  |  |
|----------------------------------|---|-----------------|----------------|---------------------|-------------|------------------------------------|-----------------|-----------|--|-------------------|--------------|-------------|--|--|
| Nº estudios                      | Diseño de estudio                                     | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones              | Obesidad        | Normopeso | Relativo (IC 95%)                              | Absoluto (IC 95%) |              |             |  |  |
| <b>Supervivencia del fármaco</b> |   |                 |                |                     |             |                                    |                 |           |  |                   |              |             |  |  |
| <b>Anti-TNF</b>                  |   |                 |                |                     |             |                                    |                 |           |  |                   |              |             |  |  |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio        | NA             | No serio            | No serio    | Ajustan por factores de confusión. | ND              | ND        | <b>HR 1,01</b><br>(IC 95% 0,63 a 1,65; p=0,95) |                   | ⊕⊕○○<br>Baja | IMPORTANTE  |  |  |

Referencias: 1. Gialouri 2023. 2. Micheroli 2017. 3. Lidong 2021. 4. Rosas 2017. 5. Ortolan 2021. 6. Al-Osami 2018. 7. Lee 2017. 8. Maas 2016. 9. Micheroli 2017. 10. Ottaviani 2012. 11. Rosas 2017.

Notas:

- a. Puntuación obtenida mediante la Escala de Newcastle Ottawa de 6 puntos (alto riesgo de sesgo).
  - b. Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.
  - c. Población asiática, con categorías de IMC diferentes: IMC bajo (<18,5); IMC normal (18,5-24); sobrepeso (IMC 24- 28); y obesidad (IMC >28).
  - d. Evaluación del riesgo de sesgo de la RS mediante herramienta ROBIS con resultado poco claro. Incluyen estudios con gran heterogeneidad clínica, analizando de forma conjunta aquellos de diseño transversal y observacionales, sin que realicen la mayoría de los estudios ajuste de resultados por posibles factores de confusión.
- \*El coeficiente  $\beta$  se interpreta al igual que se hace con una diferencia de medias. Es decir, muestra la diferencia del valor medio extraído del modelo.

Pregunta: Sobre peso/obesidad vs. normopeso

| Nº estudios                      | Diseño de estudio   | Riesgo de sesgo    | Inconsistencia | Evaluación de certeza |                    |   | Nº de pacientes | Efecto              |   | Certeza  | Importancia      |
|----------------------------------|---|--------------------|----------------|-----------------------|--------------------|---|-----------------|---------------------|---|--|------------------|
|                                  |   |                    |                | Evidencia indirecta   | Imprecisión        | Otras consideraciones   |                 | Sobre peso/obesidad | Normopeso                                 |  |                  |
| <b>ASDAS</b>                     |   |                    |                |                       |                    |   |                 |                     |   |  |                  |
| 1                                | RS <sup>1</sup><br>(5 estudios observacionales <sup>2,6</sup> )   | Serio <sup>a</sup> | No serio       | No serio              | No serio           | Ajustan por factores de confusión.                                | ND              | ND                  |   | Diferencia de medias -0,19<br>(IC 95% -0,29 a -0,09) | ⊕○○○<br>Muy baja |
| <b>BASDAI</b>                    |   |                    |                |                       |                    |   |                 |                     |   |  |                  |
| 1                                | RS <sup>1</sup><br>(10 estudios observacionales <sup>2,11</sup> ) | Serio <sup>a</sup> | No serio       | No serio              | No serio           | No ajustan por factores de confusión.                             | 1.280           | 1.224               |   | Diferencia de medias -0,39 (IC 95% -0,56 a -0,21)    | ⊕○○○<br>Muy baja |
| <b>mSASSS</b>                    |   |                    |                |                       |                    |   |                 |                     |   |  |                  |
| 1                                | Estudio observacional <sup>12</sup>                               | No serio           | NA             | No serio              | Serio <sup>b</sup> | No ajustan por factores de confusión.<br>Tamaño muestral pequeño. | 18              | 12                  | OR 0,57<br>(IC 95% 0,11 a 3,04; p=0,51)   |  | ⊕○○○<br>Muy baja |
| <b>Supervivencia del fármaco</b> |   |                    |                |                       |                    |   |                 |                     |   |  |                  |
| <b>Anti-TNF</b>                  |   |                    |                |                       |                    |   |                 |                     |   |  |                  |
| 1                                | RS <sup>13</sup> (estudio observacional <sup>14</sup> )           | Serio <sup>c</sup> | NA             | No serio              | Serio <sup>d</sup> | No ajustan por factores de confusión.                             | ND              | ND                  | OR 4,35<br>(IC 95% 1,01 a 18,69; p=0,048) |  | ⊕○○○<br>Muy baja |

Referencias: 1. Ortolan 2021. 2. Hernández-Breijo 2019. 3. Maas 2016. 4. Micheroli 2017. 5. Rosas 2017. 6. Rubio-Vargas 2016. 7. Al-Osami 2018. 8. Durcan 2012. 9. Lee 2017. 10. O'Shea 2015. 11. Ottaviani 2012. 12. Pedersen 2019. 13. Gialouri 2023. 14. Hwang 2016.

Notas:

a. Evaluación del riesgo de sesgo de la RS mediante herramienta ROBIS con resultado poco claro. Incluyen estudios con gran heterogeneidad clínica, analizando de forma conjunta aquellos de diseño transversal y observacionales, sin que realicen la mayoría de los estudios ajuste de resultados por posibles factores de confusión.

b. El intervalo de confianza es amplio e incluye la no significación estadística.

c. Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.

d. El intervalo de confianza es muy amplio.

Pregunta: Obesidad vs. no obesidad.

| Evaluación de certeza |  |                    |                    |                     |                    |   | Nº de pacientes |             | Efecto  |  | Certeza          | Importancia |
|-----------------------|--|--------------------|--------------------|---------------------|--------------------|---|-----------------|-------------|---|--|------------------|-------------|
| Nº estudios           | Diseño de estudio  | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión        | Otras consideraciones   | Obesidad        | No obesidad | Relativo (IC 95%)   | Absoluto (IC 95%)  |                  |             |
| <b>ASAS 40</b>        |  |                    |                    |                     |                    |   |                 |             |   |  |                  |             |
| 1                     | RS <sup>1</sup> (estudio observacional <sup>2</sup> )        | No serio           | NA                 | No serio            | NA                 | Ajustan por factores de confusión.  | ND              | ND          |   | %ASAS40:<br>- Normopeso: 44%<br>- Sobre peso: 40%<br>- Obesidad: 29%<br><b>p=0,02</b>                | ⊕⊕○○<br>Baja     | CRÍTICA     |
| <b>ASDAS</b>          |  |                    |                    |                     |                    |   |                 |             |   |  |                  |             |
| 2                     | RS <sup>1</sup> (2 estudios observacionales <sup>2,3</sup> ) | Serio <sup>a</sup> | Serio <sup>b</sup> | No serio            | Serio <sup>c</sup> | Ajustan por factores de confusión.<br>-----<br>Diseño transversal.<br>No ajustan sus resultados.<br>Bajo tamaño muestral. | ND              | ND          | ASDAS ≤2,1:<br>OR 4,64<br>(IC 95% 1,02<br>a 24,13;<br><b>p=0,02</b> )                     | Mejoría ASDAS<br>≥1,1:<br>- Normopeso: 59%<br>- Sobre peso: 46%<br>- Obesidad: 37%<br><b>p=0,003</b> | ⊕○○○<br>Muy baja | CRÍTICA     |
|                       |  |                    |                    |                     |                    |   |                 |             | ASDAS <1,3:<br>- Normopeso: 29%<br>- Sobre peso: 15%<br>- Obesidad: 10%<br><b>p=0,001</b> |  |                  |             |

| Evaluación de certeza            |   |                    |                    |                     |                    |   | Nº de pacientes |             | Efecto  |   | Certeza          | Importancia |
|----------------------------------|---|--------------------|--------------------|---------------------|--------------------|---|-----------------|-------------|---|---|------------------|-------------|
| Nº estudios                      | Diseño de estudio   | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión        | Otras consideraciones   | Obesidad        | No obesidad | Relativo (IC 95%)   | Absoluto (IC 95%)   |                  |             |
| <b>BASDAI</b>                    |   |                    |                    |                     |                    |   |                 |             |   |   |                  |             |
| 2                                | RS <sup>1</sup> (2 estudios observacionales <sup>2,3)</sup> | Serio <sup>a</sup> | Serio <sup>b</sup> | No serio            | Serio <sup>c</sup> | Ajustan por factores de confusión.<br>-----<br>Diseño transversal.<br>No ajustan sus resultados.<br>Bajo tamaño muestral. | ND              | ND          | BASDAI ≤4:<br>OR 3,5<br>(IC 95% 0,84 a<br>17,19;<br>p=0,05).  | %BASDAI50:<br>- Normopeso:<br>48%<br>- Sobre peso:<br>40%<br>- Obesidad: 33%<br>p=0,006 | ⊕○○○<br>Muy baja | IMPORTANTE  |
| <b>Supervivencia del fármaco</b> |   |                    |                    |                     |                    |   |                 |             |   |   |                  |             |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>3)</sup>        | Serio <sup>a</sup> | NA                 | No serio            | No serio           | Diseño transversal.<br>No ajustan sus resultados.<br>Bajo tamaño muestral.  | ND              | ND          | Duración del tratamiento años media (DE)<br>- Obesos: 1,01 (0,79)<br><br>- No obesos: 1,85 (1,65)<br>p=0,08 | ⊕○○○<br>Muy baja  | IMPORTANTE       |             |

| Evaluación de certeza |   |                    |                |                     |             |                       | Nº de pacientes |             | Efecto   |  | Certeza          | Importancia |
|-----------------------|---|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|-------------|--|--|------------------|-------------|
| Nº estudios           | Diseño de estudio                                     | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Obesidad        | No obesidad | Relativo (IC 95%)  | Absoluto (IC 95%)  |                  |             |
| <b>Anti-IL17</b>      |   |                    |                |                     |             |                       |                 |             |  |  |                  |             |
| 1                     | RS <sup>1</sup> (estudio observacional <sup>4</sup> ) | Serio <sup>d</sup> | NA             | No serio            | No serio    |                       | ND              | ND          | Riesgo de interrupción<br><b>HR 0,45</b><br>(IC 95% 0,27 a 0,90;<br>$p= 0,008$ ) | Tasa de interrupción %<br>29% obesos vs.<br>50% no obesos<br>$p=0,013$ | ⊕○○○<br>Muy baja | IMPORTANTE  |

Referencias: 1. Gialouri 2023. 2. Micheroli 2017. 3. Rosas 2017. 4. Armagan 2022.

Notas:

- a. La evaluación de la calidad del estudio de Rosas et. mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS tiene como resultado un riesgo de sesgo intermedio.
- b. Existen diferencias entre los resultados de los distintos estudios.
- c. En uno de los estudios, el tamaño muestral es pequeño y los intervalos de confianza son muy amplios.
- d. Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.

## Treatment of psoriatic arthritis

### Treatment with biologic and targeted synthetic disease-modifying antirheumatic drugs

#### Clinical question

In PsA, what is the efficacy of IL-23 and IL-17 inhibitors and tsDMARDs (JAK inhibitors and apremilast) in treating axial and peripheral disease, enthesitis and dactylitis?

Pregunta: IL-17 comparado con placebo

| Nº de estudios                  | Diseño de estudio  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Evaluación de certeza |                  | Nº de pacientes                   | Efecto   |                   | Certeza | Importancia |
|---------------------------------|--------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------------|------------------|-----------------------------------|--|-------------------|---------|-------------|
|                                 |                    |                 |                |                     |             |                       | IL-17                 | PBO              |                                   | Relativo (95% CI)                                  | Absoluto (95% CI) |         |             |
| <b>ACR 20 (12-24 semanas)</b>   |                    |                 |                |                     |             |                       |                       |                  |                                   |  |                   |         |             |
| 11                              | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 1763/3382 (52.1%)     | 361/1634 (22.1%) | <b>RR 2.37</b><br>(2.15 a 2.60)   | <b>303 más por 1000</b><br>(de 254 más a 353 más ) | ⊕⊕⊕○<br>Moderado  | CRÍTICO |             |
| <b>ACR 50 (12-24 semanas)</b>   |                    |                 |                |                     |             |                       |                       |                  |                                   |  |                   |         |             |
| 10                              | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 976/3073 (31.8%)      | 118/1475 (8.0%)  | <b>RR 3.95</b><br>(3.30 a 4.73)   | <b>236 más por 1000</b><br>(de 184 más a 298 más ) | ⊕⊕⊕○<br>Moderado  | CRÍTICO |             |
| <b>ACR 70 (12 a 24 semanas)</b> |                    |                 |                |                     |             |                       |                       |                  |                                   |  |                   |         |             |
| 7                               | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 454/1759 (25.8%)      | 18/806 (2.2%)    | <b>RR 10.85</b><br>(4.43 a 26.56) | <b>220 más por 1000</b><br>(de 77 más a 571 más )  | ⊕⊕⊕○<br>Moderado  | CRÍTICO |             |

| Evaluación de certeza |                   |                 |                |                     |             |                       | Nº de pacientes |     | Efecto            |                   | Certeza | Importancia |
|-----------------------|-------------------|-----------------|----------------|---------------------|-------------|-----------------------|-----------------|-----|-------------------|-------------------|---------|-------------|
| Nº de estudios        | Diseño de estudio | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | IL-17           | PBO | Relativo (95% CI) | Absoluto (95% CI) |         |             |

#### Resolución entesitis (16 a 24 semanas)

|   |                    |       |             |             |             |         |                  |                 |                                 |   |                  |         |
|---|--------------------|-------|-------------|-------------|-------------|---------|------------------|-----------------|---------------------------------|---|------------------|---------|
| 9 | ensayos aleatorios | serio | no es serio | no es serio | no es serio | ninguno | 915/2041 (44.8%) | 274/974 (28.1%) | <b>RR 1.77</b><br>(1.35 a 2.33) | <b>217 más por 1000</b><br>(de 98 más a 374 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO |
|---|--------------------|-------|-------------|-------------|-------------|---------|------------------|-----------------|---------------------------------|---|------------------|---------|

#### Resolución dactilitis (16 a 24 semanas)

|   |                    |       |             |             |             |         |                  |                 |                                 |  |                  |         |
|---|--------------------|-------|-------------|-------------|-------------|---------|------------------|-----------------|---------------------------------|--|------------------|---------|
| 8 | ensayos aleatorios | serio | no es serio | no es serio | no es serio | ninguno | 667/1340 (49.8%) | 156/601 (26.0%) | <b>RR 2.13</b><br>(1.48 a 3.05) | <b>293 más por 1000</b><br>(de 125 más a 532 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO |
|---|--------------------|-------|-------------|-------------|-------------|---------|------------------|-----------------|---------------------------------|--|------------------|---------|

CI: Intervalo de confianza; RR: Riesgo relativo; PBO: Placebo

#### Explicaciones:

Se ha disminuido un nivel por riesgo de sesgo dado que en varios de los ensayos clínicos no está clara si hicieron una ocultación de la asignación y en dos de ellos no se describe la generación de la secuencia de aleatorización (Anexo V).

Pregunta: IL-23 comparado con placebo

| Evaluación de certeza                     |                    |                 |                |                     |             |                       | Nº de pacientes  |                  | Efecto                       |   | Certeza          | Importancia |
|---|--------------------|-----------------|----------------|---------------------|-------------|-----------------------|------------------|------------------|------------------------------|---|------------------|-------------|
| Nº de estudios                            | Diseño de estudio  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | IL-23            | PBO              | Relativo (95% CI)            | Absoluto (95% CI)                               |                  |             |
| <b>ACR 20 (24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                  |                              |   |                  |             |
| 5   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 933/1644 (56.8%) | 347/1168 (29.7%) | <b>RR 1.92</b> (1.70 a 2.17) | <b>273 más por 1000</b> (de 208 más a 348 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 50 (24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                  |                              |   |                  |             |
| 5   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 501/1644 (30.5%) | 125/1168 (10.7%) | <b>RR 2.82</b> (2.36 a 3.39) | <b>195 más por 1000</b> (de 146 más a 256 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 70 (24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                  |                              |   |                  |             |
| 5   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 235/1644 (14.3%) | 54/1168 (4.6%)   | <b>RR 3.04</b> (2.27 a 4.07) | <b>94 más por 1000</b> (de 59 más a 142 más )   | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución entesitis (24 semanas)</b>  |                    |                 |                |                     |             |                       |                  |                  |                              |   |                  |             |
| 5   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 615/1451 (42.4%) | 312/1096 (28.5%) | <b>RR 1.47</b> (1.31 a 1.64) | <b>134 más por 1000</b> (de 88 más a 182 más )  | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución dactilitis (24 semanas)</b> |                    |                 |                |                     |             |                       |                  |                  |                              |   |                  |             |
| 5   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 439/1180 (37.2%) | 229/945 (24.2%)  | <b>RR 1.35</b> (1.18 a 1.53) | <b>85 más por 1000</b> (de 44 más a 128 más )   | ⊕⊕⊕○<br>Moderado | CRÍTICO     |

CI: Intervalo de confianza; RR: Riesgo relativo; PBO: Placebo

**Explicaciones:** Se ha disminuido un nivel por riesgo de sesgo dado que en varios de los ensayos clínicos no está clara si hicieron una ocultación de la asignación y si hubo un cegamiento de la variable de resultado (Anexo V).

Pregunta: JAKi comparado con placebo

| Evaluación de certeza                     |                    |                 |                |                     |             |                       | Nº de pacientes   |                 | Efecto                           |  | Certeza          | Importancia |
|---|--------------------|-----------------|----------------|---------------------|-------------|-----------------------|-------------------|-----------------|----------------------------------|--|------------------|-------------|
| Nº de estudios                            | Diseño de estudio  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | JAKi              | PBO             | Relativo (95% CI)                | Absoluto (95% CI)                                  |                  |             |
| <b>ACR 20 (12 semanas)</b>                |                    |                 |                |                     |             |                       |                   |                 |                                  |  |                  |             |
| 4   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 1138/1755 (64.8%) | 270/871 (31.0%) | <b>RR 2.07</b><br>(1.82 a 2.36)  | <b>332 más por 1000</b><br>(de 254 más a 422 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 50 (12 semanas)</b>                |                    |                 |                |                     |             |                       |                   |                 |                                  |  |                  |             |
| 4   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 677/1755 (38.6%)  | 95/871 (10.9%)  | <b>RR 3.54</b><br>(2.15 a 5.82)  | <b>277 más por 1000</b><br>(de 125 más a 526 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 70 (12 semanas)</b>                |                    |                 |                |                     |             |                       |                   |                 |                                  |  |                  |             |
| 4   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 302/1755 (17.2%)  | 29/871 (3.3%)   | <b>RR 4.83</b><br>(1.67 a 13.97) | <b>128 más por 1000</b><br>(de 22 más a 432 más )  | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución entesitis (12 semanas)</b>  |                    |                 |                |                     |             |                       |                   |                 |                                  |  |                  |             |
| 3   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 540/1135 (47.6%)  | 141/543 (26.0%) | <b>RR 1.80</b><br>(1.54 a 2.10)  | <b>208 más por 1000</b><br>(de 140 más a 286 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución dactilitis (12 semanas)</b> |                    |                 |                |                     |             |                       |                   |                 |                                  |  |                  |             |
| 3   | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 407/634 (64.2%)   | 110/311 (35.4%) | <b>RR 1.83</b><br>(1.56 a 2.14)  | <b>294 más por 1000</b><br>(de 198 más a 403 más ) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |

CI: Intervalo de confianza; RR: Riesgo relativo; PBO: Placebo

Explicaciones: Se ha disminuido un nivel en la dimensión de riesgo de sesgo porque no está clara la generación aleatoria de la secuencia ni la ocultación de la asignación y hay riesgo alto de resultados incompletos (Anexo V).

Pregunta: Apremilast comparado con placebo

| Evaluación de certeza                          |                    |                 |                |                     |             |                       | Nº de pacientes  |                 | Efecto                       |   | Certeza          | Importancia |
|--|--------------------|-----------------|----------------|---------------------|-------------|-----------------------|------------------|-----------------|------------------------------|---|------------------|-------------|
| Nº de estudios                                 | Diseño de estudio  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Apremilast       | PBO             | Relativo (95% CI)            | Absoluto (95% CI)                             |                  |             |
| <b>ACR 20 (16 a 24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                 |                              |   |                  |             |
| 5  | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 445/1446 (30.8%) | 130/778 (16.7%) | <b>RR 1.87</b> (1.57 a 2.23) | <b>145 más por 1000</b> (de 95 más a 206 más) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 50 (16 a 24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                 |                              |   |                  |             |
| 5  | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 203/1446 (14.0%) | 42/778 (5.4%)   | <b>RR 2.58</b> (1.79 a 3.71) | <b>85 más por 1000</b> (de 43 ms a 146 más)   | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>ACR 70 (16 a 24 semanas)</b>                |                    |                 |                |                     |             |                       |                  |                 |                              |   |                  |             |
| 5  | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 69/1446 (4.8%)   | 8/778 (1.0%)    | <b>RR 3.74</b> (1.64 a 8.52) | <b>28 más por 1000</b> (de 7 más a 77 más)    | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución entesitis (16 a 24 semanas)</b>  |                    |                 |                |                     |             |                       |                  |                 |                              |   |                  |             |
| 3  | ensayos aleatorios | serio           | no es serio    | no es serio         | no es serio | ninguno               | 158/491 (32.2%)  | 53/263 (20.2%)  | <b>RR 1.63</b> (1.24 a 2.14) | <b>127 más por 1000</b> (de 48 más a 230 más) | ⊕⊕⊕○<br>Moderado | CRÍTICO     |
| <b>Resolución dactilitis (16 a 24 semanas)</b> |                    |                 |                |                     |             |                       |                  |                 |                              |   |                  |             |
| 2  | ensayos aleatorios | no es serio     | no es serio    | no es serio         | no es serio | ninguno               | 130/295 (44.1%)  | 55/156 (35.3%)  | <b>RR 1.25</b> (0.98 a 1.60) | <b>88 más por 1000</b> (de 7 menos a 212 más) | ⊕⊕⊕○<br>Alta     | CRÍTICO     |

CI: Intervalo de confianza; RR: Riesgo relativo; PBO: Placebo

Explicaciones: Se ha disminuido un nivel en la dimensión de riesgo de sesgo porque no está clara la generación aleatoria de la secuencia ni la ocultación de la asignación en algunos de los ensayos (Anexo V).

## Treatment with biologic or targeted synthetic disease-modifying antirheumatic drugs compared to TNF inhibitors

### Clinical question

In PsA, what is the efficacy, effectiveness and safety of IL-17, IL-23 and JAK inhibitors compared to TNF inhibitors?

### Secukinumab vs adalimumab (52 semanas)

| Nº estudios           | Diseño | Evaluación de la calidad |                |                    |             |                   |                 | Nº de pacientes | Efecto                        |   | Calidad          | Importancia         |
|-----------------------|--------|--------------------------|----------------|--------------------|-------------|-------------------|-----------------|-----------------|-------------------------------|---|------------------|---------------------|
|                       |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión | Sesgo publicación | Secukinumab     |                 | Adalimumab                    | Relativo (95% IC)                         |                  |                     |
| <b>ACR20</b>          |        |                          |                |                    |             |                   |                 |                 |                               |   |                  |                     |
| 1                     | ECA    | no serio                 | NA             | no serio           | serio       | no serio          | 285/426 (67%)   | 265/427 (62%)   | <b>RR 1,08</b><br>(0,98-1,19) | 48 más por mil<br>(de 15 menos a 118 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| <b>ACR50</b>          |        |                          |                |                    |             |                   |                 |                 |                               |   |                  |                     |
| 1                     | ECA    | no serio                 | NA             | no serio           | serio       | no serio          | 209/426 (49%)   | 192/427 (45%)   | <b>RR 1,09</b><br>(0,95-1,26) | 41 más por mil<br>(de 24 menos a 116 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| <b>ACR70</b>          |        |                          |                |                    |             |                   |                 |                 |                               |   |                  |                     |
| 1                     | ECA    | no serio                 | NA             | no serio           | serio       | no serio          | 141/426 (33%)   | 124/427 (29%)   | <b>RR 1,09</b><br>(0,94-1,25) | 39 más por mil<br>(de 26 menos a 113 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| <b>DAPSA remisión</b> |        |                          |                |                    |             |                   |                 |                 |                               |   |                  |                     |
| 1                     | ECA    | no serio                 | NA             | no serio           | serio       | no serio          | 106,5/426 (25%) | 103/427 (24%)   | <b>RR 1,04</b><br>(0,82-1,32) | 10 más por mil<br>(de 43 menos a 77 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| <b>MDA</b>            |        |                          |                |                    |             |                   |                 |                 |                               |   |                  |                     |
| 1                     | ECA    | no serio                 | NA             | no serio           | serio       | no serio          | 183/426 (43%)   | 162/427 (38%)   | <b>RR 1,13</b><br>(0,96-1,33) | 50 más por mil<br>(de 14 menos a 126 más) | ⊕⊕⊕○<br>MODERADA | MENOS<br>IMPORTANTE |

| Resolución entesitis (LEI=0)  |     |          |    |          |       |          |                |               |                        |  |                  |         |
|-------------------------------|-----|----------|----|----------|-------|----------|----------------|---------------|------------------------|--|------------------|---------|
| 1                             | ECA | no serio | NA | no serio | serio | no serio | 143/234 (61%)  | 143/264 (54%) | RR 1,13<br>(0,97-1,31) | 128 más por mil<br>(de 16 menos a 169 más) | ⊕⊕⊕○<br>MODERADA | CRITICA |
| Resolución dactilitis (LDI=0) |     |          |    |          |       |          |                |               |                        |  |                  |         |
| 1                             | ECA | no serio | NA | no serio | serio | no serio | 97,5/130 (75%) | 96/137 (70%)  | RR 1,08<br>(0,93-1,25) | 53 más por mil<br>(de 50 menos a 173 más)  | ⊕⊕⊕○<br>MODERADA | CRITICA |
| Eventos adversos              |     |          |    |          |       |          |                |               |                        |  |                  |         |
| 1                             | ECA | no serio | NA | no serio | serio | No serio | 330/426 (77%)  | 338/427 (79%) | RR 0,98<br>(0,91-1,05) | 17 menos por mil<br>(de 70 menos a 40 más) | ⊕⊕⊕○<br>MODERADA | CRITICA |
| Eventos adversos graves       |     |          |    |          |       |          |                |               |                        |  |                  |         |
| 1                             | ECA | no serio | NA | no serio | serio | No serio | 32/426 (8%)    | 28/427 (7%)   | RR 1,15<br>(0,70-1,87) | 10 más por mil<br>(de 20 menos a 57 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA |
| Infecciones totales           |     |          |    |          |       |          |                |               |                        |  |                  |         |
| 1                             | ECA | no serio | NA | no serio | serio | No serio | 237/426 (56%)  | 234/427 (55%) | RR 1,02<br>(0,90-1,15) | 15 más por mil<br>(de 55 menos a 80 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA |
| Infecciones graves            |     |          |    |          |       |          |                |               |                        |  |                  |         |
| 1                             | ECA | no serio | NA | no serio | serio | No serio | 7/426 (2%)     | 6/427 (1%)    | RR 1,17<br>(0,40-3,45) | 2 más por mil (de 8 menos a 34 más)        | ⊕⊕⊕○<br>MODERADA | CRITICA |

|             |     |          |    |          |       |          |             |   |   |               |                  |         |
|-------------|-----|----------|----|----------|-------|----------|-------------|---|---|---------------|------------------|---------|
|             |     |          |    |          |       |          |             |   |   |               |                  |         |
| <b>MACE</b> |     |          |    |          |       |          |             |   |   |               |                  |         |
| 1           | ECA | no serio | NA | no serio | serio | No serio | 2/426 (<1%) | 0 | - | 5 más por mil | ⊕⊕⊕○<br>MODERADA | CRITICA |

|                   |     |          |    |          |       |          |             |            |                               |  |                  |         |
|-------------------|-----|----------|----|----------|-------|----------|-------------|------------|-------------------------------|--|------------------|---------|
| <b>Neoplasias</b> |     |          |    |          |       |          |             |            |                               |  |                  |         |
| 1                 | ECA | no serio | NA | no serio | serio | No serio | 2/426 (<1%) | 3/427 (1%) | <b>RR 0,67</b><br>(0,11-3,98) | 2 menos por mil<br>(de 6 menos a 21 más) | ⊕⊕⊕○<br>MODERADA | CRITICA |
| <b>IBD</b>        |     |          |    |          |       |          |             |            |                               |  |                  |         |
| 1                 | ECA | no serio | NA | no serio | serio | No serio | 2/426 (<1%) | 0          | -                             | 5 más por mil                            | ⊕⊕⊕○<br>MODERADA | CRITICA |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio; MACE: eventos cardiovasculares mayores, IBD: enfermedad inflamatoria intestinal

**Explicaciones:**

a) IC95% que cruza la línea del no efecto.

**Referencia:**

McInnes IB et al. Secukinumab vs adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial. Lancet 2020; 395:1496-505.

### Ixekizumab vs adalimumab (24 y 52 semanas)

| Nº estudios                        | Diseño | Evaluación de la calidad |                |                    |                    |                   |                 | Nº de pacientes |                     | Efecto                                   |              | Calidad | Importancia |
|------------------------------------|--------|--------------------------|----------------|--------------------|--------------------|-------------------|-----------------|-----------------|---------------------|--|--------------|---------|-------------|
|                                    |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Ixekizumab      | Adalimumab      | Relativo (95% IC)   | Absoluto (95% IC)                        |              |         |             |
| <b>ACR20 (24 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 195/283 (68,9%) | 204/283 (72,1%) | RR 0,96 (0,86-1,06) | 44 menos por mil (de 101 menos a 46 más) | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>ACR20 (52 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 197/283 (69,6%) | 195/283 (68,9%) | RR 1,01 (0,91-1,13) | 7 más por mil (de 65 menos a 88 más)     | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>ACR50 (24 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 143/283 (50,5%) | 132/283 (46,6%) | RR 1,08 (0,91-1,28) | 39 más por mil (de 40 menos a 132 más)   | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>ACR50 (52 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 141/283 (49,8%) | 141/283 (49,8%) | RR 1,00 (0,85-1,18) | 0 (de 76 menos a 90 más)                 | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>ACR70 (24 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 90/283 (31,8%)  | 73/283 (25,8%)  | RR 1,23 (0,95-1,60) | 60 más por mil (de 13 menos a 155 más)   | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>ACR70 (52 semanas)</b>          |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 100/283 (35,3%) | 97/283 (34,3%)  | RR 1,03 (0,82-1,29) | 11 más por mil (de 61 menos a 100 más)   | ⊕⊕○○<br>BAJA | CRÍTICA |             |
| <b>DAPSA remisión (24 semanas)</b> |        |                          |                |                    |                    |                   |                 |                 |                     |  |              |         |             |
| 1                                  | ECA    | Serio <sup>a</sup>       | NA             | No serio           | Serio <sup>b</sup> | No serio          | 75/283 (26,5%)  | 51/283 (18%)    | RR 1,47 (1,07-2,02) | 85 más por mil (de 13 más a 183 más)     | ⊕⊕○○<br>BAJA | CRÍTICA |             |

| DAPSA remisión (52 semanas)                  |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
|--|-----|--------------------|----|----------|--------------------|----------|-----------------|-----------------|-------------------------------|--|--------------|---------|
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 85/283 (30%)    | 80/283 (28,3%)  | <b>RR 1,06</b><br>(0,82-1,37) | 18 más por mil (de 50 menos a 106 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| DAPSA baja actividad o remisión (24 semanas) |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 174/283 (61,5%) | 171/283 (60,4%) | <b>RR 1,02</b><br>(0,89-1,16) | 11 más por mil (de 65 menos a 97 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| DAPSA baja actividad o remisión (52 semanas) |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 174/283 (61,5%) | 166/283 (58,7%) | <b>RR 1,05</b><br>(0,92-1,20) | 28 más por mil (de 49 menos a 117 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| MDA (24 semanas)                             |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 135/283 (47,7%) | 100/283 (35,3%) | <b>RR 1,35</b><br>(1,11-1,65) | 124 más por mil (de 38 más a 229 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| MDA (52 semanas)                             |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 134/283 (47,3%) | 116/283 (41%)   | <b>RR 1,16</b><br>(0,96-1,39) | 64 más por mil (de 17 menos a 161 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| PASDAS remisión (24 semanas)                 |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 82/283 (29,0%)  | 55/283 (19,4%)  | <b>RR 1,49</b><br>(1,11-2,01) | 95 más por mil (de 21 más a 197 más)   | ⊕⊕○○<br>BAJA | CRÍTICA |
| PASDAS baja actividad (24 semanas)           |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 164/283 (58%)   | 147/283 (51,9%) | <b>RR 1,12</b><br>(0,96-1,30) | 60 más por mil (de 21 menos a 154 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| Resolución entesitis (LEI=0) (24 semanas)    |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 95/159 (59,7%)  | 81/147 (55,1%)  | <b>RR 1,08</b><br>(0,89-1,32) | 46 más por mil (de 59 menos a 174 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| Resolución entesitis (LEI=0) (52 semanas)    |     |                    |    |          |                    |          |                 |                 |                               |  |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 98/283 (61,6%)  | 84/283 (57,1%)  | <b>RR 1,17</b><br>(0,92-1,48) | 49 más por mil (de 25 menos a 144 más) | ⊕⊕○○<br>BAJA | CRÍTICA |

| Resolución entesitis (SPARCC=0) (24 semanas) |     |                    |    |          |                    |          |                 |                |                        |                                       |              |         |
|--|-----|--------------------|----|----------|--------------------|----------|-----------------|----------------|------------------------|---------------------------------------|--------------|---------|
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 107/189 (56,6%) | 77/171 (45%)   | RR 1,26<br>(1,02-1,55) | 116 más por mil (de 10 más a 246 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| Resolución entesitis (SPARCC=0) (52 semanas) |     |                    |    |          |                    |          |                 |                |                        |                                       |              |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 107/283 (56,6%) | 83/283 (48,5%) | RR 1,29<br>(1,02-1,63) | 85 más por mil (de 6 más a 185 más)   | ⊕⊕○○<br>BAJA | CRÍTICA |

| Resolución dactilitis (LDI=0) (24 semanas) |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
|--|-----|--------------------|----|----------|--------------------|----------|-----------------|-----------------|------------------------|--|-----------------------|---------|
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 37/42 (88,1%)   | 54/58 (93,1%)   | RR 0,95<br>(0,83-1,08) | 54 menos por mil (de 159 menos a 74 más)   | ⊕⊕○○<br>BAJA          | CRÍTICA |
| Resolución dactilitis (LDI=0) (52 semanas) |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 35/283 (83,3%)  | 47/283 (81,0%)  | RR 0,74<br>(0,50-1,12) | 42 más por mil (de 84 menos a 19 más)      | ⊕⊕○○<br>BAJA          | CRÍTICA |
| Eventos adversos totales (24 semanas)      |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 197/283 (69,6%) | 173(283 (61,1%) | RR 1,14<br>(1,01-1,28) | 85 más por mil (de 6 más a 174 más)        | ⊕⊕○○<br>BAJA          | CRÍTICA |
| Eventos adversos totales (52 semanas)      |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 209/283 (73,9%) | 194(283 (68,6%) | RR 1,08<br>(0,97-1,20) | 53 más por mil (de 21 menos a 135 más)     | ⊕⊕○○<br>BAJA          | CRÍTICA |
| Eventos adversos graves (24 semanas)       |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | No serio           | No serio | 10/283 (3,5%)   | 24/283 (8,5%)   | RR 0,42<br>(0,20-0,86) | 49 menos por mil (de 68 menos a 12 menos)  | ⊕⊕○○<br>BAJA-MODERADA | CRÍTICA |
| Eventos adversos graves (52 semanas)       |     |                    |    |          |                    |          |                 |                 |                        |  |                       |         |
| 1  | ECA | Serio <sup>a</sup> | NA | No serio | No serio           | No serio | 12/283 (4,2%)   | 35/283 (12,4%)  | RR 0,34<br>(0,18-0,65) | 81 menos por mil (de 101 menos a 44 menos) | ⊕⊕○○<br>BAJA-MODERADA | CRÍTICA |

|   |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
|---|-----|--------------------|----|----------|--------------------|----------|---------------|-----------------|-------------------------------|---|--------------|---------|
|   |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| <b>Infecciones totales (24 semanas)</b> |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 102/283 (36%) | 87/283 (30,7%)  | <b>RR 1,17</b><br>(0,93-1,48) | 53 más por mil (de 22 menos a 148 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>Infecciones totales (52 semanas)</b> |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 119/283 (42%) | 111/283 (39,2%) | <b>RR 1,07</b><br>(0,88-1,31) | 28 más por mil (de 48 menos a 121 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>Infecciones graves (24 semanas)</b>  |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 4/283 (1,4%)  | 8/283 (2,8%)    | <b>RR 0,50</b><br>(0,15-1,64) | 14 menos por mil (de 24 menos a 18 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>Infecciones graves (52 semanas)</b>  |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 5/283 (1,8%)  | 8/283 (2,8%)    | <b>RR 0,63</b><br>(0,21-1,89) | 11 menos por mil (de 22 menos a 25 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>MACE (24 semanas)</b>                |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 3/283 (1,1%)  | 5/283 (1,8%)    | <b>RR 0,60</b><br>(0,14-2,49) | 7 menos por mil (de 15 menos a 26 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>MACE (52 semanas)</b>                |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 5/283 (1,8%)  | 7/283 (2,5%)    | <b>RR 0,71</b><br>(0,23-2,22) | 7 menos por mil (de 19 menos a 30 más)  | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>Neoplasias (24 semanas)</b>          |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 0             | 3/283 (1,1%)    | -                             | 11 menos por mil                        | ⊕⊕○○<br>BAJA | CRÍTICA |
| <b>Neoplasias (52 semanas)</b>          |     |                    |    |          |                    |          |               |                 |                               |   |              |         |
| 1                                       | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 0             | 4/283 (1,4%)    | -                             | 14 menos por mil                        | ⊕⊕○○<br>BAJA | CRÍTICA |

| Depresión (24 semanas) |     |                    |    |          |                    |          |              |              |                        |  |              |         |
|------------------------|-----|--------------------|----|----------|--------------------|----------|--------------|--------------|------------------------|--|--------------|---------|
| 1                      | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 3/283 (1,1%) | 7/283 (2,5%) | RR 0,43<br>(0,11-1,64) | 14 menos por mil (de 22<br>menos a 16 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| Depresión (52 semanas) |     |                    |    |          |                    |          |              |              |                        |  |              |         |
| 1                      | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 5/283 (1,8%) | 9/283 (3,2%) | RR 0,56<br>(0,19-1,64) | 14 menos por mil (de 26<br>menos a 20 más) | ⊕⊕○○<br>BAJA | CRÍTICA |
| IBD (24 semanas)       |     |                    |    |          |                    |          |              |              |                        |  |              |         |
| 1                      | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 2/283 (0,7%) | 0            | -                      | 7 más por mil                              | ⊕⊕○○<br>BAJA | CRÍTICA |
| IBD (52 semanas)       |     |                    |    |          |                    |          |              |              |                        |  |              |         |
| 1                      | ECA | Serio <sup>a</sup> | NA | No serio | Serio <sup>b</sup> | No serio | 2/283 (0,7%) | 0            | -                      | 7 más por mil                              | ⊕⊕○○<br>BAJA | CRÍTICA |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio, MACE: eventos cerebrocardiovasculares; IBD: enfermedad inflamatoria intestinal

**Explicaciones:**

a. Los pacientes sabían qué tratamiento estaban recibiendo. Es posible que hayan informado a los investigadores, mientras les estaban evaluando

b. IC95% que cruza la línea del no efecto.

**Referencias:**

Mease PJ et al. A head-to head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial. Ann Rheum Dis 2020; 79:123-31.

Smolen JS et al. Multicentre, randomised, open-label, parallel-group study evaluating the efficacy and safety of ixekizumab vs adalimumab in patients with psoriatic arthritis naïve to biological disease-modifying antirheumatic drug: final results by week 52. Ann Rheum Dis 2020; 79: 1310-9.

## Bimekizumab vs adalimumab (16 y 24 semanas)

| Evaluación de la calidad |        |                 |                |                    |                    |                   | Nº de pacientes |              | Efecto              |   | Calidad          | Importancia |
|--------------------------|--------|-----------------|----------------|--------------------|--------------------|-------------------|-----------------|--------------|---------------------|---|------------------|-------------|
| Nº estudios              | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Bimekizumab     | Adalimumab   | Relativo (95% IC)   | Absoluto (95% IC)                         |                  |             |
| <b>ACR20 (semana 16)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 268/431 (62%)   | 96/140 (69%) | RR 0,91 (0,79-1,04) | 64 más por mil (de 142 menos a 25 más)    | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>ACR20 (semana 24)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 282/431 (65%)   | 99/140 (71%) | RR 0,93 (0,82-1,05) | 53 menos por mil (de 131 menos a 36 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>ACR50 (semana 16)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 189/431 (44%)   | 64/140 (46%) | RR 0,96 (0,78-1,18) | 19 menos por mil (de 102 menos a 84 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>ACR50 (semana 24)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 196/431 (45%)   | 66/140 (47%) | RR 0,82 (0,67-1,01) | 85 menos por mil (de 156 menos a 2,5 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>ACR70 (semana 16)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 105/431 (24%)   | 39/140 (28%) | RR 0,87 (0,64-1,20) | 35 menos por mil (de 101 menos a 55 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>ACR70 (semana 24)</b> |        |                 |                |                    |                    |                   |                 |              |                     |   |                  |             |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 126/431 (29%)   | 42/140 (30%) | RR 0,97 (0,73-1,31) | 8 menos por mil (de 82 menos a 92 más)    | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |

| MDA (semana 16)                          |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
|--|-----|----------|----|----------|--------------------|----------|---------------|--------------|-------------------------------|---|------------------|------------------|
| 1  | ECA | no serio | NA | No serio | no serio           | No serio | 194/431 (45%) | 63/140 (45%) | <b>RR 0,69</b><br>(0,56-0,86) | 0 (de 85 menos a 106 más)                 | ⊕⊕⊕⊕<br>ALTA     | MENOS IMPORTANTE |
| MDA (semana 24)                          |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 209/431 (48%) | 67/140 (48%) | <b>RR 1,01</b><br>(0,83-1,24) | 13 más por mil (de 81 menos a 113 más)    | ⊕⊕⊕○<br>MODERADA | MENOS IMPORTANTE |
| Resolución entesitis (LEI=0) (semana 16) |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 124/249 (50%) | 18/36 (50%)  | <b>RR 0,77</b><br>(0,54-1,09) | 115 menos por mil (de 229 menos a 46 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Eventos adversos totales) (semana 24)    |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 300/431 (70%) | 96/140 (69%) | <b>RR 1,02</b><br>(0,89-1,15) | 10 más por mil (de 74 menos a 106 más)    | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Eventos adversos graves (semana 16)      |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 4/431 (1%)    | 3/140 (2%)   | <b>RR 0,43</b><br>(0,10-1,91) | 12 menos por mil (de 19 menos a 20 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Eventos adversos graves (semana 24)      |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 9/431 (1%)    | 3/140 (2%)   | <b>RR 0,97</b><br>(0,27-3,55) | 1 más por mil (de 16 menos a 55 más)      | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Infecciones totales (semana 16)          |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 131/431 (30%) | 35/140 (25%) | <b>RR 1,22</b><br>(0,88-1,68) | 54 más por mil (de 29 menos a 169 más)    | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Infecciones totales (semana 24)          |     |          |    |          |                    |          |               |              |                               |   |                  |                  |
| 1  | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 170/431 (39%) | 41/140 (29%) | <b>RR 1,35</b><br>(1,02-1,79) | 102 más por mil (de 4 más a 231 más)      | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| Infecciones graves (semana 16)           |     |          |    |          |                    |          |               |              |                               |   |                  |                  |

|                                       |     |          |    |          |                    |          |             |            |                               |  |                  |         |
|---------------------------------------|-----|----------|----|----------|--------------------|----------|-------------|------------|-------------------------------|--|------------------|---------|
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/431 (<1%) | 1/140 (1%) | <b>RR 0,32</b><br>(0,02-5,16) | 5 menos por mil (de 7 menos a 30 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>Infecciones graves (semana 24)</b> |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 3/431 (1%)  | 2/140 (1%) | <b>RR 0,49</b><br>(0,08-2,89) | 7 menos por mil (de 13 menos a 27 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>MACE (semana 16)</b>               |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 0           | 0          | -                             | -                                      | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>MACE (semana 24)</b>               |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/431 (1%)  | 0          | -                             | 7 más por mil                          | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>Neoplasias (semana 16)</b>         |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/431 (<1%) | 0          | -                             | 2 más por mil                          | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>Neoplasias (semana 24)</b>         |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 2/431 (<1%) | 0          | -                             | 5 más por mil                          | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>IBD (semana 16)</b>                |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 0           | 0          | -                             | -                                      | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>IBD (semana 24)</b>                |     |          |    |          |                    |          |             |            |                               |  |                  |         |
| 1                                     | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/431 (<1%) | 0          | -                             | 2 más por mil                          | ⊕⊕⊕○<br>MODERADA | CRÍTICA |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio, NI: no hay información, MACE: eventos cerebrocardiovasculares; IBD: enfermedad inflamatoria intestinal

**Explicaciones:**

a. IC95% que cruza la línea del no efecto.

**Referencias:**

McInnes IB et al. Bimekizumab in patients with psoriatic arthritis, naïve to biological treatment: a randomised, double-blind, placebo-controlled, phase 3 trial (BE OPTIMAL). Lancet 2023; 401: 25-37.

## Ustekinumab vs anti-TNF (24 semanas)

| Evaluación de la calidad |        |                        |                   |                    |                    |                   | Nº de pacientes, mediana (RIQ) |              | Efecto            |                   | Calidad         | Importancia |
|--------------------------|--------|------------------------|-------------------|--------------------|--------------------|-------------------|--------------------------------|--------------|-------------------|-------------------|-----------------|-------------|
| Nº estudios              | Diseño | Riesgo sesgo           | de Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | antiIL12/23 N=23               | AntiTNF N=24 | Relativo (95% IC) | Absoluto (95% IC) |                 |             |
| <b>DAPSA</b>             |        |                        |                   |                    |                    |                   |                                |              |                   |                   |                 |             |
| 1<br>n=47<br>pacientes   | ECA    | Muy Serio <sup>a</sup> | NA                | no serio           | serio <sup>b</sup> | no serio          | 3,61 (4,54)                    | 6,88 (6,22)  | NI <sup>c</sup>   | NI <sup>c</sup>   | ⊕⊕⊕<br>MUY BAJA | IMPORTANTE  |
| <b>BASDAI</b>            |        |                        |                   |                    |                    |                   |                                |              |                   |                   |                 |             |
| 1<br>n=47<br>pacientes   | ECA    | Serio <sup>a</sup>     | NA                | no serio           | serio <sup>b</sup> | no serio          | 0,4 (0,75)                     | 1,1 (1,55)   | NI <sup>c</sup>   | NI <sup>c</sup>   | ⊕⊕⊕<br>MUY BAJA | IMPORTANTE  |
| <b>LEI</b>               |        |                        |                   |                    |                    |                   |                                |              |                   |                   |                 |             |
| 1<br>n=47<br>pacientes   | ECA    | Serio <sup>a</sup>     | NA                | no serio           | serio <sup>b</sup> | no serio          | 0 (0)                          | 0,5 (1)      | NI <sup>c</sup>   | NI <sup>c</sup>   | ⊕⊕⊕<br>MUY BAJA | CRÍTICA     |
| <b>LDI</b>               |        |                        |                   |                    |                    |                   |                                |              |                   |                   |                 |             |
| 1<br>n=47<br>pacientes   | ECA    | Serio <sup>a</sup>     | NA                | no serio           | serio <sup>b</sup> | no serio          | 0 (0)                          | 0 (0)        | NI <sup>c</sup>   | NI <sup>c</sup>   | ⊕⊕⊕<br>MUY BAJA | CRÍTICA     |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; NI: No indicado; RR: Risk ratio, RIQ: rango intercuartílico

### Explicaciones:

a. No hay ningún tipo de cegamiento, número pequeño de pacientes, diseño del estudio etc

b. No se proporcionan IC y no se pueden calcular con los datos proporcionados

c. No se puede calcular el efecto relativo ni absoluto al no proporcionarse el número de pacientes en ambos grupos de tratamiento y para cada una de las variables. Sólo se proporcionan los datos en forma de mediana y RIQ y valores de p

### Referencias:

Araujo EG et al. Effects of ustekinumab vs tumor necrosis factor inhibition on enthesitis: Results from the enthesial clearance in psoriatic arthritis (ECLIPSA) study. Semin Arthritis Rheum 2019; 48: 632-7.

## Guselkumab Q8W 100 mg vs anti-TNF

| Nº estudios                         | Diseño  | Evaluación de la calidad |                |                    |             |                   | n/% pacientes/eventos o media±DE o mediana (rango) |                                    | Efecto  |                   | Calidad          | Importancia |
|-------------------------------------|---|--------------------------|----------------|--------------------|-------------|-------------------|--|------------------------------------|---|-------------------|------------------|-------------|
|                                     |   | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión | Sesgo publicación | Guselkumab   | antiTNF                            | Relativo (RR, 95% IC)   | Absoluto (95% IC) |                  |             |
| <b>ACR20</b>                        |   |                          |                |                    |             |                   |  |                                    |   |                   |                  |             |
| 1 revisión sistemática (5 estudios) | 1 ECA<br>ADEPT (GUSE vs ADA 40 mg, 12 semanas)            | Serio                    | No serio       | Serio              | No serio    | No serio          | GUS 59%  | ADA 57%                            | RR 1,05 (0,85, 1,27)  | NI                | ⊕⊕○○<br>BAJA     | CRÍTICA     |
|                                     | 1 ECA<br>(GUSE vs ETA 25 mg 24 semanas)                   | Serio                    | No serio       | Serio              | No serio    | No serio          | GUS 59%  | ETA 59%                            | RR 0,98 (0,73, 1,36)  | NI                | ⊕⊕○○<br>BAJA     | CRÍTICA     |
|                                     | 1 ECA<br>GO-REVEAL (GUSE vs GOL 50 mg, 14 semanas)        | No serio                 | No serio       | Serio              | No serio    | No serio          | GUS 59%  | GOL 48%                            | RR 0,88 (0,64, 1,22)  | NI                | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
|                                     | 1 ECA<br>RAPID-PSA (GUSE vs CZP 200 y 400 mg, 12 semanas) | No serio                 | No serio       | Serio              | No serio    | No serio          | GUS 59%  | CZP 400 mg 51,9%<br>CZP 200 mg 58% | CZP 400 mg<br>RR 1,11 (0,84, 1,48)<br>CZP 200 mg<br>RR 0,99 (0,77,1,30) | NI                | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
|                                     | 1 ECA<br>IMPACT-2 (GUSE vs IFX 5 mg/Kg, 14 semanas)       | No serio                 | No serio       | Serio              | No serio    | No serio          | GUS 59%  | IFX 58%                            | RR 0,82 (0,61, 1,11)  | NI                | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
| <b>vdH-S score</b>                  |   |                          |                |                    |             |                   |  |                                    |   |                   |                  |             |
| 1 revisión sistemática (5 estudios) | 1 ECA<br>ADEPT (GUSE vs ADA 40 mg, 12 semanas)            | Serio                    | No serio       | Serio              | No serio    | No serio          | GUS  | ADA                                | MD -0,04 (-0,58, 0,50)  | NI                | ⊕⊕○○<br>BAJA     | CRÍTICA     |
|                                     | 1 ECA<br>(GUSE vs ETA 25 mg 24 semanas)                   | Serio                    | No serio       | Serio              | No serio    | No serio          | GUS  | ETA                                | MD 0,13 (-0,43, 0,69)   | NI                | ⊕⊕○○<br>BAJA     | CRÍTICA     |
|                                     | 1 ECA<br>GO-REVEAL (GUSE vs GOL 50 mg, 14 semanas)        | No serio                 | No serio       | Serio              | No serio    | No serio          | GUS  | GOL                                | MD 0,00 (-0,58, 0,56)   | NI                | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |
|                                     | 1 ECA<br>RAPID-PSA (GUSE vs CZP 200 y 400 mg, 12 semanas) | No serio                 | No serio       | Serio              | No serio    | No serio          | GUS  | CZP                                | CZP 400 mg<br>MD -0,26 (-0,79, 0,27)<br>CZP 200 mg                      | NI                | ⊕⊕⊕○<br>MODERADA | CRÍTICA     |

|  |   |          |          |       |                               |          |     |                              |                             |    |                  |         |
|--|---|----------|----------|-------|-------------------------------|----------|-----|------------------------------|-----------------------------|----|------------------|---------|
|  |   |          |          |       |                               |          |     | <b>MD -0,15 (-0,68,0,37)</b> |                             |    |                  |         |
|  | 1 ECA<br>IMPACT-2 (GUSE vs IFX 5 mg/Kg, 14 semanas) | No serio | No serio | Serio | No serio<br>Rheumatology 2021 | No serio | GUS | IFX                          | <b>MD 1,09 (0,23, 1,96)</b> | NI | ⊕⊕⊕○<br>MODERADA | CRÍTICA |

| Cualquier AEs                       |   |          |          |       |          |          |     |  |  |    |                  |         |
|-------------------------------------|---|----------|----------|-------|----------|----------|-----|--|--|----|------------------|---------|
| 1 revisión sistemática (4 estudios) | 1 ECA<br>ADEPT (GUSE vs ADA 40 mg, 12 semanas)            | Serio    | No serio | Serio | No serio | No serio | GUS | ADA NI                                   | <b>RR 0,96 (0,78, 1,16)</b>  | NI | ⊕⊕○○<br>BAJA     | CRÍTICA |
|                                     | 1 ECA<br>GO-REVEAL (GUSE vs GOL 50 mg, 14 semanas)        | No serio | No serio | Serio | No serio | No serio | GUS | GOL 65%                                  | <b>RR 0,78 (0,62, 0,99)</b>  | NI | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
|                                     | 1 ECA<br>RAPID-PSA (GUSE vs CZP 200 y 400 mg, 12 semanas) | No serio | No serio | Serio | No serio | No serio | GUS | CZP 400 mg (71,1%)<br>CZP 200 mg (68,1%) | CZP 400 mg<br><b>RR 0,77 (0,62, 0,99)</b><br>CZP 200 mg<br><b>RR 0,82 (0,63, 1,06)</b> | NI | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
|                                     | 1 ECA<br>IMPACT-2 GUSE vs (IFX 5 mg/Kg, 14 semanas)       | No serio | No serio | Serio | No serio | No serio | GUS | IFX 67%                                  | <b>RR 0,68 (0,55, 0,87)</b>  | NI | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
|                                     |   |          |          |       |          |          |     |  |  |    |                  |         |

Q8W: cada 8 semanas; vdH-S Score: van der Heijde-Sharp Score; AEs: acontecimientos adversos; NI: no informado; IC: Intervalo de confianza; ADA: adalimumab; GOL: golimumab; ETA: etanercept; IFX: infliximab; CZP: certolizumab pegol

**Explicaciones:**

**AMSTAR de la revisión sistemática críticamente baja** por cuanto que los pacientes incluidos con duración del tratamiento distinta, heterogeneidad de los estudios incluidos aunque no hay pruebas estadísticas que la evalúen; se incluyen algunos estudios en los que no hay cegamiento claro, no está claro el método utilizado para evaluar los datos perdidos en varios de los estudios incluidos, diferente duración de los estudios etc

Además, no hay estudios *head to head* de guselkumab vs antiTNF, se comparó de forma indirecta la eficacia de guselkumab vs placebo en cuanto a ACR20, vdH-S score y AEs y la eficacia de los antiTNF vs placebo en las mismas variables

**Referencias:**

Méase P et al.; 60:2009-21.

## UPADACITINIB 15 mg vs ADALIMUMAB 12 SEMANAS

| Nº estudios                                 | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Nº de pacientes   |                 | Efecto              |  | Calidad       | Importancia   |
|---|--------|-----------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|---------------------|--|---------------|---------------|
|   |        |                 |                |                    |                    |                   | Upadacitinib 15mg | Adalimumab      | Relativo (95% IC)   | Absoluto (95% IC)                        |               |               |
| ACR-20 ( semana 12)                         |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 302/429 (70,4%)   | 278/429 (65%)   | RR 1,04 (0,95-1,14) | 41 menos por 1000 (de 32 menos a 94 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| ACR 50 ( semana12)                          |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 160/429 (37,5%)   | 160/429 (37,5%) | RR 1 (0,84-1,19)    | 0 (de 59 menos a 70 más)                 | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| ACR 70 ( semana12)                          |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 67/429 (15,6%)    | 59/429(13,8%)   | RR 1,14 (0,82-1,57) | 19 menos por 1000 (de 24 menos a 78 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| MDA ( semana 12)                            |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | NO Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 106/429 (24,7%)   | 107/429(24,9%)  | RR 1 (0,79 a 1,26)  | 0 (de 51 menos a 65 más)                 | ⊕⊕⊕○ MODERADA | NO IMPORTANTE |
| LEI=0 ( semana 12)                          |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 127/270 (47,4%)   | 124/265 (46,8%) | RR 1,01 (0,84-1,20) | 2 menos por 1000 (de 75 menos a 95 más)  | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| LDI=0 (semana12)                            |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 100/136 (73,5%)   | 91/127 (71,7%)  | RR 1,03 (0,88-1,19) | 19 menos por mil (de 82 menos a 136 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| ASDAS ( cambio medio 12 s respecto basal )  |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                  | NI                                       | ⊕⊕⊕○ MODERADA | IMPORTANTE    |
| BASDAI ( cambio medio 12 s respecto basal ) |        |                 |                |                    |                    |                   |                   |                 |                     |  |               |               |
| 1   | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                  | NI                                       | ⊕⊕⊕○ MODERADA | IMPORTANTE    |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información. Serio<sup>a</sup>: . IC95% que cruza la línea del no efecto:

### UPADACITINIB 15mg vs adalimumab (24 semanas)

| Nº estudios  | Diseño | Evaluación de la calidad |                |                    |                    |                   | Nº de pacientes   |                 | Efecto                |   | Calidad          | Importancia      |
|--|--------|--------------------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|-----------------------|---|------------------|------------------|
|  |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 15mg | Adalimumab      | Relativo (95% IC)     | Absoluto (95% IC)                         |                  |                  |
| <b>ACR-20 ( semana 24)</b>                         |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 327/429 (76,3%)   | 307/429(71,6%)  | RR 1,07 (0,98-1,15)   | 47 menos por 1000 (de 11 menos a 109 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR 50 ( semana 24)</b>                         |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | NO Serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 224/429 (52,2,%)  | 190/429(44,3%)  | RR 1,18 (1,03-1,36)   | 79 menos por 1000 (de 11 más a 157 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR 70 ( semana 24)</b>                         |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | NO Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 121/429 (28,4%)   | 97/429(22,6%)   | RR 1,25 (0,99-1,57)   | 56 menos por 1000 (de 2 menos a 129 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>MDA ( semana 24)</b>                            |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 157/429 (36,6%)   | 142/429 (33,3%) | RR 1,11 (0,92 a 1,33) | 35 menos por 1000 (de 26 menos a 108 más) | ⊕⊕⊕○<br>MODERADA | MENOS IMPORTANTE |
| <b>LEI=0 ( semana 24)</b>                          |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | No serio           | no serio          | 145/270 (53,7%)   | 125/265 (47,2%) | RR 1,14 (0,96-1,35)   | 65 menos por 1000 (de 18 menos a 164 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>LDI=0 ( semana 24)</b>                          |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 104/136 (76,5%)   | 94/127 (74%)    | RR 1,03 (0,90-1,19)   | 25 menos por mil (de 74 menos a 138 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ASDAS ( cambio medio 24 s respecto basal )</b>  |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | IMPORTANTE       |
| <b>BASDAI ( cambio medio 24 s respecto basal )</b> |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | IMPORTANTE       |
| <b>No progresión radiográfica (mTSS ≤0)</b>        |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No Serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 313/322 (97,2%)   | 308/320 (96,3%) | RR 1,00 (0,92-1,09)   | 1 menos por mil ( de 55 menos a 63 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA          |
| <b>No progresión radiográfica (mTSS ≤0,5)</b>      |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                  |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 317/322(98,4%)    | 314/320 (98,1%) | RR 1 (0,92-1,02)      | 3 menos por mil (de 59 menos a 57 más)    | ⊕⊕⊕○<br>MODERADA | CRITICA          |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio; NI: No información; Serio<sup>a</sup>: . IC95% que cruza la línea del no efecto (**Iain B. McInnes et all; N Engl J Med 2021;384:1227-39.**)

### UPADACITINIB 15mg vs adalimumab (56 semanas) .

| Nº estudios                                      | Diseño | Evaluación de la calidad |                |                    |                    |                   | Nº de pacientes   |                 | Efecto                |   | Calidad       | Importancia   |
|--|--------|--------------------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|-----------------------|---|---------------|---------------|
|  |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 15mg | Adalimumab      | Relativo (95% IC)     | Absoluto (95% IC)                         |               |               |
| <b>ACR-20 ( semana 56)</b>                       |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | No serio           | no serio          | 319/429 (74,4%)   | 292/429 (68,1%) | RR 1,09 (1-1,19)      | 63 menos por 1000 (de 2 más a 129 más)    | ⊕⊕⊕⊕ ALTA     | CRÍTICA       |
| <b>ACR 50 ( semana 56)</b>                       |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 256/429 (59,7%)   | 218/429 (51%)   | RR 1,17 (1,04-1,33)   | 89 menos por 1000 (de 20 más a 165 más)   | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>ACR 70 ( semana 56)</b>                       |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 174/429 (40,6%)   | 133/429 (31,2%) | RR 1,31 (1,09-1,57)   | 96 menos por 1000 (de 28 más a 176 más)   | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>MDA ( semana 56)</b>                          |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 192/429 (44,80%)  | 169/429 (39,6%) | RR 1,14 (0,97 a 1,33) | 54 menos por 1000 (de 11 menos a 129 más) | ⊕⊕⊕○ MODERADA | NO IMPORTANTE |
| <b>LEI=0 ( semana 56)</b>                        |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 160/270 (59,3%)   | 143/265(54%)    | RR 1,10 (0,95-1,27)   | 53 menos por 1000 (de 28 menos a 148 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>LDI=0 (semana 56)</b>                         |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 102/136 (75%)     | 94/127 (74%)    | RR 1,01 (0,88-1,17)   | 10 menos por mil (de 89 menos a 123 más)  | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>ASDAS (cambio medio 12 s respecto basal)</b>  |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○ MODERADA | IMPORTANTE    |
| <b>BASDAI (cambio medio 24 s respecto basal)</b> |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○ MODERADA | IMPORTANTE    |
| <b>No progresión radiográfica (mTSS ≤0)</b>      |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 309/320 (96,60%)  | 283/301 (94%)   | RR 1,08 (0,98-1,18)   | 51 menos por mil (de 10 menos a 118 más)  | ⊕⊕⊕○ MODERADA | CRITICA       |
| <b>No progresión radiográfica (mTSS ≤0,5)</b>    |        |                          |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | NO serio                 | NA             | no serio           | Serio <sup>a</sup> | serio             | 313/320 (97,80%)  | 287/301(95,30%) | RR 1,08 (0,99-1,17)   | 51 menos por mil (de 9 menos a 117 más)   | ⊕⊕⊕○ MODERADA | CRITICA       |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

(McInnes et all; Rheumatol Ther, 2022: p. 1-18.)

UPADACITINIB 15mg VS ADALIMUMAB (104 SEMANAS)

| Evaluación de la calidad                     |        |                 |                |                    |                    |                   | Nº de pacientes   |                  | Efecto                |   | Calidad          | Importancia     |
|--|--------|-----------------|----------------|--------------------|--------------------|-------------------|-------------------|------------------|-----------------------|---|------------------|-----------------|
| Nº estudios                                  | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 15mg | Adalimumab       | Relativo (95% IC)     | Absoluto (95% IC)                         |                  |                 |
| ACR-20 ( semana 104)                         |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 296/429 (69%)     | 272/429 (63,4%)  | RR 1,09 (0,99-1,20)   | 56 menos por 1000 (de 7 menos a 125 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| ACR 50 ( semana 104)                         |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 289 /429 (53,6%)  | 230/429(47,1%)   | RR 1,26 (1,13-1,40)   | 138 menos por 1000 (de 67 más a 215 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| 9ACR 70 ( semana 104)                        |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 163/429 (38%)     | 126/429(29,4%)   | RR 1,29 (1,07-1,56)   | 86 menos por 1000 (de 20 más a 165 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| MDA ( semana 104)                            |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 180/429(42%)      | 162/429 (37,8%)  | RR 1,11 (0,94 a 1,31) | 42 menos por 1000 (de 21 menos a 117 más) | ⊕⊕⊕○<br>MODERADA | MENOS RELEVANTE |
| LEI=0 ( semana 104)                          |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 144/270(53,3%)    | 130/265(49,1%)   | RR 1,09 (0,92-1,28)   | 43 menos por 1000 (de 38 menos a 138 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| LDI=0 (semana 104)                           |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No Serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 95/136 (69,9%)    | 92/127 (72,4%)   | RR 0,96 (0,83-1,12)   | 26 más por mil (de 125 menos a 90 más)    | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| ASDAS ( cambio medio 104 s respecto basal )  |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI               | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | RELEVANTE       |
| BASDAI ( cambio medio 104 s respecto basal ) |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI               | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | RELEVANTE       |
| No progression radiográfica ( mTSS ≤0 )      |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 312/324 (96,30%)  | 300/320(93,80%)  | 1,03 (0,94-1,2)       | 18 menos por mil (de 40 menos a 81 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA         |
| No progression radiográfica ( mTSS ≤0,5 )    |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 316/324 (97,50%)  | 305/320 (95,30%) | RR 1,02 (0,94-1,11)   | 16 menos por mil (de 42 menos a 78 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA         |
| Infecciones graves                           |        |                 |                |                    |                    |                   |                   |                  |                       |   |                  |                 |

|               |     |          |    |          |                    |          |         |         |                                |  |                  |         |
|---------------|-----|----------|----|----------|--------------------|----------|---------|---------|--------------------------------|--|------------------|---------|
| 1             | ECA | NO serio | NA | no serio | Serio <sup>a</sup> | no serio | 27/617  | 9/429   | <b>RR 2,09</b><br>(0,99-4,39)  | 23 menos por mil (de 0,18<br>menos a 71 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA |
| MACES         |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | NO serio | NA | no serio | Serio <sup>a</sup> | no serio | 3/617   | 2/429   | <b>RR 1,04</b><br>(0,18-6,22)  | 0 (de 3 menos a 24 más)                        | ⊕⊕⊕○<br>MODERADA | CRITICA |
| VTE           |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | No serio | NA | No serio | Serio <sup>a</sup> | No serio | 2/617   | 2/429   | <b>RR 1,04</b><br>(0,18-6,22)  | 0 más por mil<br>( de<br>3 menos a 24 más)     | ⊕⊕⊕○<br>MODERADA | CRITICA |
| HEPATOPATIA   |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | No serio | NA | no serio | No serio           | No serio | 193/617 | 167/429 | <b>RR 0,80</b><br>(0,68-0,95)  | 76 más por mil<br>(de<br>124 menos a 19 menos) | ⊕⊕⊕⊕<br>ALTA     | CRITICA |
| NEOPLASIA     |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | No serio | NA | no serio | Serio <sup>a</sup> | No serio | 14/617  | 6/429   | <b>RR 1,62</b><br>(0,63-4,19)  | 9 menos por mil<br>(de<br>5 menos a 44 más)    | ⊕⊕⊕○<br>MODERADA | CRITICA |
| HERPES ZOSTER |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | No serio | NA | no serio | Serio <sup>b</sup> | No serio | 37/617  | 3/429   | <b>RR 8,58</b><br>(2,66-27,63) | 53 menos por mil (de 11 más a<br>186 más)      | ⊕⊕⊕○<br>MODERADA | CRITICA |
| AUMENTO CPK   |     |          |    |          |                    |          |         |         |                                |  |                  |         |
| 1             | ECA | No serio | NA | no serio | Serio <sup>b</sup> | No serio | 114/617 | 52/429  | <b>RR 1,52</b><br>(1,12-2,07)  | 64 menos por mil<br>(de<br>15 más a 129 más)   | ⊕⊕⊕○<br>MODERADA | CRITICA |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información

Serio<sup>a</sup> : Calidad rebajada un nivel por imprecisión IC95% que cruza la línea del no efecto; Serio<sup>b</sup>: Calidad rebajada un nivel por imprecisión. IC95% que cruza el umbral del efecto clínicamente relevante (McInnes et all; Rheumatol Ther, 2022: p. 1-18.)

### Upadacitinib 30mg vs adalimumab (semana 12)

| Nº estudios  | Diseño | Evaluación de la calidad |                |                    |                    |                   | Nº de pacientes   |                 | Efecto                |   | Calidad          | Importancia     |
|--|--------|--------------------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|-----------------------|---|------------------|-----------------|
|  |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 30mg | Adalimumab      | Relativo (95% IC)     | Absoluto (95% IC)                         |                  |                 |
| <b>ACR-20 ( semana 12)</b>                           |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 332/423 (78,7%)   | 278/429 (65%)   | RR 1,21 (1,11-1,32)   | 137 menos por 1000 (de 72 más a 207 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| <b>ACR 50 ( semana 12)</b>                           |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 219 /423 (51,8%)  | 160/429 (37,5%) | RR 1,39 (1,19-1,62)   | 145 menos por 1000 (de 71 más a 230 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| <b>ACR 70 ( semana 12)</b>                           |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 107/423 (25,30%)  | 59/429(13,8%)   | RR 1,84 (1,38-2,45)   | 115 menos por 1000 (de 52 más a 199 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| <b>MDA ( semana 12)</b>                              |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>b</sup> | no serio          | 150/423(35,50%)   | 107/429(24,9%)  | RR 1,42 (1,15 a 1,75) | 105 menos por 1000 (de 38 más a 187 más)  | ⊕⊕⊕○<br>MODERADA | MENOS RELEVANTE |
| <b>LEI=0 ( semana 12)</b>                            |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 138/268(51,5%)    | 124/265 (46,0%) | RR 1,10 (0,93-1,31)   | 47 menos por 1000 (de 34 menos a 144 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| <b>LDI=0 (semana 12)</b>                             |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | No serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | 101/127(79,5%)    | 95/127(71,7%)   | RR 1,06 (0,93-1,22)   | 47 menos por mil (de 52 menos a 161 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA         |
| <b>ASDAS ( cambio medio 12 s respecto basal )</b>    |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | NO serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | RELEVANTE       |
| <b>BASDAI ( CAMBIO MEDIO 12 S RESPECTO A BASAL )</b> |        |                          |                |                    |                    |                   |                   |                 |                       |   |                  |                 |
| 1  | ECA    | NO serio                 | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○<br>MODERADA | RELEVANTE       |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

(Iain B. McInnes et al; N Engl J Med 2021;384:1227-39.)

### Upadacitinib 30mg vs adalimumab (semana 24)

| Evaluación de la calidad                   |        |                 |                |                    |                    |                   | Nº de pacientes   |                 | Efecto                |  | Calidad       | Importancia   |
|--|--------|-----------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|-----------------------|--|---------------|---------------|
| Nº estudios                                | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 30mg | Adalimumab      | Relativo (95% IC)     | Absoluto (95% IC)                        |               |               |
| ACR-20 ( semana 24)                        |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | No serio           | no serio          | 332/423(78,5%)    | 307/429(71,6%)  | RR 1,10 (1,01-1,19)   | 69 menos por 1000 (de 10 más a 132 más)  | ⊕⊕⊕⊕ ALTA     | CRÍTICA       |
| ACR 50 ( semana 24)                        |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 255 /423 (60,5%)  | 190/429(44,3%)  | RR 1,36 (1,19-1,55)   | 160 menos por 1000 (de 85 más a 244 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| ACR 70 ( semana 24)                        |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 153/423(36,4%)    | 97/429(22,6%)   | RR 1,60 (1,29-1,99)   | 136 menos por 1000 (de 65 más a 222 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| MDA ( semana 24)                           |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 192/423(45,40%)   | 142/429 (33,3%) | RR 1,37 (1,16 a 1,63) | 123 menos por 1000 (de 51 más a 207 más) | ⊕⊕⊕○ MODERADA | NO IMPORTANTE |
| LEI=0 ( semana 24)                         |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 100/268 (57,5%)   | 125/265 (47,2%) | RR 1,34 (1,17-1,53)   | 181 menos por 1000 (de 90 más a 284 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| LDI=0 ( semana 24)                         |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 101/127 (79,5%)   | 94/127 (74%)    | RR 1,07 (0,94-1,23)   | 55 menos por mil (de 45 menos a 170 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| ASDAS ( cambio medio 24 s respecto basal ) |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI                                       | ⊕⊕⊕○ MODERADA | RELEVANTE     |
| BASDAI ( CAMBIO MEDIO 24s respecto basal ) |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI                                       | ⊕⊕⊕○ MODERADA | RELEVANTE     |
| No progression radiográfica ( mTSS ≤0)     |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 316/325 (97,20%)  | 308/320(96,3%)  | RR 1,01 (0,98-1,04)   | 10 menos por mil (de 17 menos a 37 más)  | ⊕⊕⊕○ MODERADA | CRITICA       |
| No progression radiográfica ( mTSS ≤0,5)   |        |                 |                |                    |                    |                   |                   |                 |                       |  |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 318/325 (98,40%)  | 314/320(98,1%)  | RR 1 (0,98-1,02)      | 3 más por mil (de 24 menos a 19 más)     | ⊕⊕⊕○ MODERADA | CRITICA       |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto. (Iain B. McInnes et all; N Engl J Med 2021;384:1227-39.)

## Upadacitinib 30mg vs adalimumab (semana 56)

| Evaluación de la calidad                           |        |                 |                |                    |                    |                   | Nº de pacientes   |                 | Efecto                |   | Calidad       | Importancia   |
|--|--------|-----------------|----------------|--------------------|--------------------|-------------------|-------------------|-----------------|-----------------------|---|---------------|---------------|
| Nº estudios  | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Upadacitinib 30mg | Adalimumab      | Relativo (95% IC)     | Absolute (95% IC)                         |               |               |
| <b>ACR-20 ( semana 56)</b>                         |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | No serio           | no serio          | 315/423 (74,50%)  | 292/429 (68,1%) | RR 1,09 (1-1,19)      | 64 menos por 1000 (de 2 más a 130 más)    | ⊕⊕⊕⊕ ALTA     | CRÍTICA       |
| <b>ACR 50 ( semana 56)</b>                         |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 261 /423 (61,9%)  | 218/429 (51%)   | RR 1,21 (1,08-1,37)   | 109 menos por 1000 (de 39 más a 187 más)  | ⊕⊕⊕○ MODERDA  | CRÍTICA       |
| <b>ACR 70 ( semana 56)</b>                         |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 184/423(43,7%)    | 133/429 (31,2%) | RR 1,40 (1,7-1,68)    | 125 menos por 1000 (de 53 más a 209 más)  | ⊕⊕⊕○ MODERDA  | CRÍTICA       |
| <b>MDA ( semana 56)</b>                            |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>b</sup> | no serio          | 200/423 (47,3%)   | 169/429 (39,6%) | RR 1,20 (1,03 a 1,40) | 79 menos por 1000 (de 11 más a 157 más)   | ⊕⊕⊕○ MODERDA  | NO IMPORTANTE |
| <b>LEI=0 ( semana 56)</b>                          |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 155/268 (57,8%)   | 143/265(54%)    | RR 1,07 (0,92-1,25)   | 39 menos por 1000 (de 42 menos a 133 más) | ⊕⊕⊕○ MODERDA  | CRÍTICA       |
| <b>LDI=0 (semana 56)</b>                           |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | 95/127 (74,8%)    | 94/127 (74%)    | RR 1,01 (0,87-1,17)   | 8 menos por mil (de 92 menos a 123 más)   | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>ASDAS ( cambio medio 56 s respecto basal )</b>  |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  |               | IMPORTANTE    |
| <b>BASDAI ( CAMBIO MEDIO 56 s respecto basal )</b> |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> | no serio          | NI                | NI              | NI                    | NI  |               | IMPORTANTE    |
| <b>No progresión radiográfica ( mTSS ≤0 )</b>      |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | no serio           | no serio          | 308/316 (97,50%)  | 283/301(94%)    | RR 1,04 (1-1,07)      | 34 menos por mil (de 2más a 67 más)       | ⊕⊕⊕⊕ ALTA     | CRITICA       |
| <b>No progresión radiográfica ( mTSS ≤0,5 )</b>    |        |                 |                |                    |                    |                   |                   |                 |                       |   |               |               |
| 1  | ECA    | No serio        | NA             | no serio           | no serio           | no serio          | 311/316 (98,40%)  | 287/301(95,3%)  | RR 1,03 (1-1,06)      | 31 menos por mil (de 2 más a 59 más)      | ⊕⊕⊕⊕ ALTA     | CRITICA       |

McInnes et all; Rheumatol Ther, 2022: p. 1-18.)

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

## Upadacitinib 30mg vs adalimumab (semana 104)

| Evaluación de la calidad                                |        |                 |                |                    |                      |                   | Nº de pacientes   |                 | Efecto                |   | Calidad       | Importancia   |
|---|--------|-----------------|----------------|--------------------|----------------------|-------------------|-------------------|-----------------|-----------------------|---|---------------|---------------|
| Nº estudios   | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión          | Sesgo publicación | Upadacitinib 30mg | Adalimumab      | Relativo (95% IC)     | Absoluto (95% IC)                         |               |               |
| <b>ACR-20 ( semana 104)</b>                             |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | No serio        | NA             | no serio           | no serio             | no serio          | 294/423(69,5%)    | 272/429 (63,4%) | RR 1,10 (1-1,21)      | 61 menos por 1000 (de 2 menos a m130 más) | ⊕⊕⊕⊕ ALTA     | CRÍTICA       |
| <b>ACR 50 ( semana 104)</b>                             |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> : | no serio          | 250 /423 (59,3%)  | 230/429(47,1%)  | RR 1,10 (0,98-1,24)   | 55 menos por 1000 (de 11 menos a 129 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>ACR 70 ( semana 104)</b>                             |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | Serio <sup>b</sup>   | no serio          | 184/423(43,5%)    | 126/429(29,4%)  | RR 1,48 (1,23-1,78)   | 141 menos por 1000 (de 68 más a 228 más)  | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>MDA ( semana 104)</b>                                |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | Serio <sup>b</sup>   | no serio          | 194/423(45,9%)    | 162/429 (37,8%) | RR 1,21 (1,04 a 1,42) | 81 menos por 1000 (de 13 más a 160 más)   | ⊕⊕⊕○ MODERADA | NO IMPORTANTE |
| <b>LEI=0 ( semana 104)</b>                              |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> : | no serio          | 139/268(52,2%)    | 130/265(49,1%)  | RR 1,06 (0,89-1,25)   | 28 menos por 1000 (de 52 menos a 123 más) | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>LDI=0 (semana 104)</b>                               |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | Serio <sup>a</sup> : | no serio          | 91/127(71,7%)     | 92/127 (72,4%)  | RR 0,99 (0,85-1,15)   | 8 menos por mil (de 109 menos a 110 más)  | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>ASDAS ( cambio medio 104s respecto basal )</b>       |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | serio                | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○ MODERADA | IMPORTANTE    |
| <b>BASDAI (cambio medio 106 semanas respecto basal)</b> |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | serio                | no serio          | NI                | NI              | NI                    | NI  | ⊕⊕⊕○ MODERADA | IMPORTANTE    |
| <b>No progresión radiográfica ( mTSS ≤0 )</b>           |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | No serio        | NA             | no serio           | Serio <sup>a</sup>   | no serio          | 311/322 (96,60%)  | 300/320(93,80%) | RR 1,03 (0,99-1,07)   | 28 menos por mil (de 4 menos a 62 más)    | ⊕⊕⊕○ MODERADA | CRÍTICA       |
| <b>No progresión radiográfica ( mTSS ≤0,5 )</b>         |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |
| 1   | ECA    | NO serio        | NA             | no serio           | no serio             | no serio          | 316/322(98,10%)   | 305/320(95,3%)  | RR 1,03 (1-1,06)      | 28 menos por mil (de 0,5 más a 56 más)    | ⊕⊕⊕⊕ ALTA     | CRÍTICA       |
| <b>Infecciones graves</b>                               |        |                 |                |                    |                      |                   |                   |                 |                       |   |               |               |

|                      |     |          |    |          |                      |          |         |         |                                |  |                  |         |
|----------------------|-----|----------|----|----------|----------------------|----------|---------|---------|--------------------------------|--|------------------|---------|
| 1                    | ECA | NO serio | NA | no serio | Serio <sup>b</sup>   | no serio | 44/613  | 9/429   | <b>RR 3,42</b><br>(1,69-9,93)  | 51 menos por mil<br>(de 14 más a 124 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>MACES</b>         |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | No serio | NA | no serio | Serio <sup>a</sup> : | no serio | 2/613   | 2/429   | <b>RR 0,70</b><br>(0,10-4,95)  | 1 más por mil<br>(de 4 menos a 18 más)     | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>VTE</b>           |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | NO serio | NA | no serio | Serio <sup>a</sup> : | no serio | 5/613   | 2/429   | <b>RR 1,75</b><br>(0,34-8,98)  | 3 menos por mil<br>(de 3 menos a 37 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>NEOPLASIAS</b>    |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | NO serio | NA | no serio | No serio             | no serio | 14/613  | 6/429   | <b>RR 1,63</b><br>(0,63-4,22)  | 9 menos por mil ( de 5 menos a 44 más)     | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>HERPES ZOSTER</b> |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | NO serio | NA | no serio | Serio <sup>c</sup>   | no serio | 61/613  | 3/429   | <b>RR 14,23</b><br>(4,49-45)   | 93 menos por mil<br>(de 24 más a 308 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>HEPATOPATIA</b>   |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | NO serio | NA | no serio | Serio <sup>a</sup> : | no serio | 219/613 | 167/429 | <b>RR 0,92</b><br>(0,78- 1,08) | 32 más por mil<br>(de 84 menos a 29 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA |
| <b>AUMENTO CPK</b>   |     |          |    |          |                      |          |         |         |                                |  |                  |         |
| 1                    | ECA | NO serio | NA | no serio | Serio <sup>b</sup>   | no serio | 176/613 | 52/429  | 2,37<br>(1,78-3,15)            | 166 menos por mil<br>(de 94 más a 260 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA |

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

(McInnes et all; Rheumatol Ther, 2022: p. 1-18.)

### Tofacitinib 5mg vs adalimumab (3 y 12 meses)

| Evaluación de la calidad |        |                 |                |                    |                    |                   | Nº de pacientes |            | Efecto               |  | Calidad          | Importancia      |
|--------------------------|--------|-----------------|----------------|--------------------|--------------------|-------------------|-----------------|------------|----------------------|--|------------------|------------------|
| Nº estudios              | Diseño | Riesgo de sesgo | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Tofacitinib 5mg | Adalimumab | Relativo (95% IC)    | Absoluto (95% IC)                        |                  |                  |
| <b>ACR20 ( 3 mes)</b>    |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 54/107          | 55/106     | RR 0,97 (0,75-1,26)  | 14 más por mil (de 130 menos a 137 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR20 ( 12 mes)</b>   |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 73/107          | 64/106     | RR 1,13 (0,92-1,38)  | 78 menos por mil (de 45 menos a 230 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR50 (3 mes)</b>     |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 30/107          | 35/106     | RR 0,85 (0,57-1,28)  | 50 más por mil (de 143 menos a 91 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR50 ( 12 mes)</b>   |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 48/107          | 43/106     | RR 1,11 (0,81-1,51)  | 43 menos por mil (de 77 menos a 207 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR70 (3 mes)</b>     |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 35/107          | 32/106     | RR 1,08 (0,73-1,61)  | 25 menos por mil (de 81 menos a 184 más) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR70 (12 mes)</b>    |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 25/107          | 32/106     | RR 0,77 (0,49-1,21)  | 68 más por mil (de 152 menos a 64 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>MDA (3 mes)</b>       |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |
| 1                        | ECA    | no serio        | NA             | No serio           | Serio <sup>a</sup> | No serio          | 28/107          | 27/106     | RR: 1,03 (0,65-1,62) | 7menos por mil ( de 88 menos a 157 mas)  | ⊕⊕⊕○<br>MODERADA | MENOS IMPORTANTE |
| <b>MDA ( 12 mes)</b>     |        |                 |                |                    |                    |                   |                 |            |                      |  |                  |                  |

|                                    |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
|------------------------------------|-----|----------|----|----------|--------------------|----------|--------|--------|------------------------------|--|------------------|---------------------|
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 40/107 | 42/106 | <b>RR: 1,47(0,98-2,21)</b>   | 119 menos por mil (de 6 menos a 307 más) | ⊕⊕⊕○<br>MODERADA | MENOS<br>IMPORTANTE |
| LEI ( 3 mes)                       |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| LEI ( 12 mes)                      |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Dactylitis Severity Score* ( 3mes) |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Dactylitis Severity Score*(12 mes) |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 94/107 | 93/106 | <b>RR:1 ( 0,91-1,11)</b>     | 1 menos por mil ( de 82 menos a 93 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| vdHm S, ( 12 mes)                  |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 94/107 | 93/106 | <b>RR: 1 ( 0,91-1,11)</b>    | 1 menos por mil ( de 82 menos a 93 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| EA grave (3 mes)                   |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 3/107  | 1/106  | <b>RR:2,97 ( 0,31-28,12)</b> | 19 menos por mil (de 6 menos a 255 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| EA grave (12 mes)                  |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 8/107  | 9/106  | <b>RR: 0,88(0,35-2,20)</b>   | 10 más por mil( de 54 menos a 101 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Herpes zoster ( 3 mes)             |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/107  | 0/106  | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Herpes zoster (12 mes)             |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 2/107  | 0/106  | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| MACES ( 3 mes)                     |     |          |    |          |                    |          |        |        |                              |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 0/107  | 0/106  | NA                           | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |

|                        |     |          |    |          |                    |          |       |       |    |    |                  |         |
|------------------------|-----|----------|----|----------|--------------------|----------|-------|-------|----|----|------------------|---------|
|                        |     |          |    |          |                    |          |       |       |    |    | MODERADA         |         |
| <b>MACES ( 12 mes)</b> |     |          |    |          |                    |          |       |       |    |    |                  |         |
| 1                      | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 0/107 | 0/106 | NA | NA | ⊕⊕⊕○<br>MODERADA | CRÍTICA |

(Mease et al Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis. New England 2017; 377; 16: 1537-1550)

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

## Tofacitinib 10mg vs adalimumab (3 y 12 meses)

| Nº estudios            | Diseño | Evaluación de la calidad |                |                    |                    |                   | Nº de pacientes  |            | Efecto              |   | Calidad          | Importancia      |
|------------------------|--------|--------------------------|----------------|--------------------|--------------------|-------------------|------------------|------------|---------------------|---|------------------|------------------|
|                        |        | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión        | Sesgo publicación | Tofacitinib 10mg | Adalimumab | Relativo (95% IC)   | Absoluto (95% IC)                         |                  |                  |
| <b>ACR20 ( 3 mes)</b>  |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 63/104           | 55/106     | RR 1,17 (0,92-1,48) | 87 menos por mil (de 42 menos a 251 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR20 ( 12 mes)</b> |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 63/104           | 64/106     | RR 1 (0,81-1,25)    | 2 menos por mil (de 116 menos a 150 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR50 ( 3 mes)</b>  |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 42/104           | 35/106     | RR 1,22 (0,86-1,75) | 74 menos por mil (de 47 menos a 247 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR50 ( 12 mes)</b> |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 50/104           | 43/106     | RR 1,19 (0,87-1,61) | 75 menos por mil (de 51 menos a 246 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR70 (3 mes)</b>   |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 15/104           | 32/106     | RR 0,48 (0,28-0,83) | 158 más por mil (de 218 menos a 51 menos) | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>ACR70 (12 mes)</b>  |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 32/104           | 31/106     | RR 1,05 (0,70-1,59) | 15 menos por mil (de 88 menos a 172 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA          |
| <b>MDA (3 mes)</b>     |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |
| 1                      | ECA    | no serio                 | NA             | No serio           | Serio <sup>a</sup> | No serio          | 27/104           | 27/106     | RR 1,02(0,64-1,61)  | 5menos por mil(de 90 menos a 156 más)     | ⊕⊕⊕○<br>MODERADA | MENOS IMPORTANTE |
| <b>MDA ( 12 mes)</b>   |        |                          |                |                    |                    |                   |                  |            |                     |   |                  |                  |

|                                    |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
|------------------------------------|-----|----------|----|----------|--------------------|----------|--------|--------|-----------------------------|--|------------------|---------------------|
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 45/104 | 42/106 | <b>RR 1,09 ( 0,79-1,51)</b> | 36 menos por mil (de 82 menos a 200 más) | ⊕⊕⊕○<br>MODERADA | MENOS<br>IMPORTANTE |
| LEI ( 3 mes)                       |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| LEI ( 12 mes)                      |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Dactylitis Severity Score* ( 3mes) |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Dactylitis Severity Score*(12 mes) |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | NA     | NA     | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| vdHm S, Nº ( 12 mes)               |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 94/104 | 93/106 | <b>RR 1,03(0,94-1,13)</b>   | 26 menos por mil(de 55 menos a 116 más)  | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| EA grave ( 3 mes)                  |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 1/104  | 1/106  | <b>RR1,02(0,06-16,08)</b>   | 0 (de 8 menos a 142 más)                 | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| EA grave (12 mes)                  |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 4/104  | 9/106  | <b>RR 0,45(0,14-1,43)</b>   | 46 más por mil ( de 72 menos a 36 más)   | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Herpes zoster ( 3 mes)             |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 0/104  | 0/106  | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| Herpes zoster (12 mes)             |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 2/104  | 0/106  | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |
| MACES ( 3 mes)                     |     |          |    |          |                    |          |        |        |                             |  |                  |                     |
| 1                                  | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 0/104  | 0/106  | NA                          | NA                                       | ⊕⊕⊕○<br>MODERADA | CRÍTICA             |

|                        |     |          |    |          |                    |          |       |       |    |    |                  |         |
|------------------------|-----|----------|----|----------|--------------------|----------|-------|-------|----|----|------------------|---------|
|                        |     |          |    |          |                    |          |       |       |    |    | MODERADA         |         |
| <b>MACES ( 12 mes)</b> |     |          |    |          |                    |          |       |       |    |    |                  |         |
| 1                      | ECA | no serio | NA | No serio | Serio <sup>a</sup> | No serio | 0/104 | 2/106 | NA | NA | ⊕⊕⊕○<br>MODERADA | CRÍTICA |

(Mease et al Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis. New England 2017; 377; 16: 1537-1550)

ECA: ensayo clínico aleatorizado; IC: Intervalo de confianza; NA: no aplica; RR: Risk ratio ; NI: No información: Serio<sup>a</sup> : . IC95% que cruza la línea del no efecto

## Metaanálisis de no progresión radiográfica de la artritis periférica

| Nº estudios                         | Diseño  | Evaluación de la calidad |                |                    |             |                   | N pacientes/eventos o media±DE o mediana (rango) |         | Efecto no progresión Rx                                       |  | Calidad               | Importancia |
|-------------------------------------|---|--------------------------|----------------|--------------------|-------------|-------------------|--|---------|---|--|-----------------------|-------------|
|                                     |   | Riesgo de sesgo          | Inconsistencia | Carácter indirecto | Imprecisión | Sesgo publicación | Biológico  | Placebo | Relativo (RR, 95% IC)   | Absoluto (95% IC)                      |                       |             |
| <b>vdH-S score</b>                  |   |                          |                |                    |             |                   |  |         |   |  |                       |             |
| 1 Revisión sistemática (8 estudios) | 1 ECA (48 semanas)<br>ADA 40 mg vs placebo  | No serio                 | No serio       | Serio              | No serio    | No serio          | 144  | 152     | 4,11 (2,10, 8,02)   | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (96 semanas)<br>ETA 25 mg vs placebo,   | No serio                 | No serio       | Serio              | No serio    | No serio          | 71   | 70      | 4,19 (1,65, 10,61)  | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (48 semanas)<br>GOL 50 mg vs placebo<br>GOL 100 mg vs placebo   | No serio                 | No serio       | Serio              | No serio    | No serio          | 132<br>137                                       | 102     | 2,21 (1,24, 3,83)<br>1,95 (1,11, 3,42)                        | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (48 semanas)<br>IFX 5mg/Kg vs placebo,  | No serio                 | No serio       | Serio              | No serio    | No serio          | 100  | 100     | 2,54 (1,13, 5,89)   | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (RAPID-PSA) 24 semanas<br>CZP 400 mg vs placebo<br>CZP 200 mg vs placebo  | No serio                 | No serio       | Serio              | No serio    | No serio          | 135<br>138                                       | 109     | 2,32 (1,14, 4,73)<br>3,55 (1,60, 7,87)                        | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (24 semanas)<br>SECU 150 mg sin DC vs placebo<br>SECU 150 mg con DC vs placebo<br>SECU 300 mg sin DC vs placebo | No serio                 | No serio       | Serio              | No serio    | No serio          | 210<br>213<br>217                                | 296     | 1,85 (1,18, 2,90)<br>1,41 (0,93, 2,16)<br>2,63 (1,62, 4,27)   | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | 1 ECA (24 semanas)<br>IXE 80 mgQ4W vs placebo<br>IXE 80 mgQ2W vs placebo<br>ADA 40 mg                                 | No serio                 | No serio       | Serio              | No serio    | No serio          | 107<br>103<br>101                                | 106     | 2,32 (1,09, 4,92)<br>5,74 (2,10, 15,71)<br>7,10 (2,37, 21,29) | NI                                     | ⊕⊕○○<br>BAJA-MODERADA | CRÍTICA     |
|                                     | 1 ECA (52 semanas)<br>UST 45 mg vs placebo<br>UST 90 mg vs placebo  | No serio                 | No serio       | Serio              | No serio    | No serio          | 284<br>289                                       | 271     | 2,20 (1,29, 3,75)<br>2,14 (1,26, 3,63)                        | NI                                     | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | antiTNF (global) vs placebo   | No serio                 | No serio       | Serio              | No serio    | No serio          | 1199   | 1143    | 2,94 (2,38, 3,63)   | 183 más por mil (de 146 más a 214 más) | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |
|                                     | Anti-IL (global) vs placebo   | No serio                 | No serio       | Serio              | No serio    | No serio          | 1789   | 2000    | 2,15 (1,69, 2,74)   | 107 más por mil (de 79 más a 131 más)  | ⊕⊕⊕○<br>MODERADA      | CRÍTICA     |

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Q8W: cada 8 semanas; vdH-S Score: van der Heijde-Sharp Score;; NI: no informado; IC: Intervalo de confianza; ADA: adalimumab; GOL: golimumab; ETA: etanercept; IFX: infliximab; CZP: certolizumab pegol, DC: dosis de inducción; SECU: secukinumab; IXE: ixekizumab; UST: ustekinumab, anti-IL: anti-interleukinas

**Explicaciones:**

AMSTAR de la revisión sistemática **críticamente baja** por cuanto que la duración de los tratamientos es distinta, heterogeneidad de los estudios incluidos, número de pacientes tratados muy variable, distinto diseño de los estudios; en alguno de los estudios incluidos no está claro si hay cegamiento o no de los investigadores, etc

Además, no hay estudios *head to head*, se comparó de forma indirecta la eficacia de los distintos biológicos vs placebo en cuanto a la no progresión radiográfica de la artritis periférica.

**Referencias:**

Wu D et al. *Rheumatology* 2020; 59:3172-80.

## Extra-musculoskeletal manifestations

### Clinical question

In PsA, what is the efficacy of bDMARDs and tsDMARDs in treating extra-musculoskeletal manifestations (uveitis, psoriasis and IBD)

### 4.1. FAME BIOLÓGICOS

#### 4.1.1. Comparación FAMEb versus placebo

##### 4.1.1.1. DLQI (12 a 24 semanas): adalimumab, certolizumab, golimumab, ustekinumab, secukinumab, ixekizumab.

| Evaluación de certeza                       |                   |                    |                    |                     |             |                       | Nº de pacientes |         | Efecto            |  | Certeza      | Importancia   |
|---|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|--|--------------|---------------|
| Nº de estudios                              | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | FAMEb           | Placebo | Relativo (95% CI) | Absoluto (95% CI)                                      |              |               |
| 1 RS <sup>(10)</sup><br>(14 brazos [8 ECA]) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 1569            | 1563    | -                 | Diferencia medias 4.36 menos (5.76 menos a 2.96 menos) | ⊕⊕⊖⊖<br>Baja | NO IMPORTANTE |

DLQI: Dermatology Life Quality Index. ECA: ensayos clínicos aleatorizados. FAMEb: fármacos antirreumáticos modificadores de enfermedad biológico. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Heterogeneidad de los resultados no explicada.

#### 4.1.2. Comparación iTNF versus placebo

##### 4.1.2.1. Respuesta PASI 75 (rango 12 a 14 semanas): adalimumab, etanercept, infliximab, golimumab.

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes |               | Efecto                 |   | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|---------------|------------------------|---|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iTNF            | Placebo       | Relativo (95% CI)      | Absoluto (95% CI)                       |              |             |
| 1 RS <sup>(6)</sup><br>(9 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 413/801 (51.6%) | 59/741 (8.0%) | RR 7.27 (4.07 a 12.98) | 499 más por 1000 (de 244 más a 954 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: psoriasis area and severity index. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>La estimación puntual varía ampliamente entre los estudios, sin explicación por el análisis de subgrupos. Se utilizó un modelo de efectos aleatorios.

#### 4.1.2.2. DLQI (12 a 24 semanas): adalimumab, certolizumab, golimumab.

| Evaluación de certeza                      |                   |                    |                    |                     |             |                       | Nº de pacientes |         | Efecto            |  | Certeza          | Importancia   |
|--|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|---------|-------------------|--|------------------|---------------|
| Nº de estudios                             | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iTNF            | Placebo | Relativo (95% CI) | Absoluto (95% CI)                                      |                  |               |
| 1 RS <sup>(10)</sup><br>(6 brazos [4 ECA]) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 565             | 561     | -                 | Diferencia medias 3,38 menos (5,53 menos a 1,23 menos) | ⊕⊕⊕⊖<br>Moderada | NO IMPORTANTE |

DLQI: Dermatology Life Quality Index. ECA: ensayos clínicos aleatorizados. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Heterogeneidad de los resultados no explicada.

#### 4.1.2.3. Enfermedad inflamatoria intestinal: número de brotes en pacientes con EII conocida (mediana de 16 semanas): adalimumab, certolizumab, golimumab, etanercept, infliximab.

| Evaluación de certeza            |                   |                    |                    |                     |             |                       | Nº de pacientes |               | Efecto      |                   | Certeza      | Importancia |
|----------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|-----------------|---------------|-------------|-------------------|--------------|-------------|
| Nº de estudios                   | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iTNF            | Placebo       | OR (95% CI) | Absoluto (95% CI) |              |             |
| 1 RS <sup>(11)</sup><br>(14 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 0/2242 (0.0%)   | 0/1442 (0.0%) | NA          | NA                | ⊕⊕⊖⊖<br>Baja | CRÍTICA     |

#### 4.1.2.4. Enfermedad inflamatoria intestinal: número de nuevos brotes en pacientes con EII no conocida (mediana de 16 semanas): adalimumab, certolizumab, golimumab, etanercept, infliximab.

|                                  |           |                    |                    |             |             |         |               |               |    |    |              |         |
|----------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|---------------|---------------|----|----|--------------|---------|
| 1 RS <sup>(11)</sup><br>(21 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | No es serio | Ninguno | 0/2242 (0.0%) | 0/1442 (0.0%) | NA | NA | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|----------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|---------------|---------------|----|----|--------------|---------|

ECA: ensayos clínicos aleatorizados. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Heterogeneidad entre los estudios y la metodología. El grupo de pacientes con espondiloartritis está integrado por espondilitis anquilosante, espondiloartritis axial no radiográfica y espondiloartritis periférica.

#### 4.1.3. Comparación iIL-17 versus placebo

##### 4.1.3.1. Respuesta PASI 75 (rango 12 a 24 semanas): secukinumab, ixekizumab.

| Evaluación de certeza          |                   |                    |                    |                     |             |                       | Nº de pacientes    |               | Efecto                    |  | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|-------------|-----------------------|--------------------|---------------|---------------------------|--|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-17A            | Placebo       | Relativo (95% CI)         | Absoluto (95% CI)                              |              |             |
| 1 RS <sup>(6)</sup><br>(2 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | No es serio | Ninguno               | 145/231<br>(62.8%) | 11/98 (11.2%) | RR 4.92<br>(1.25 a 19.32) | 440 más por 1000<br>(de 28 más a 1000<br>más ) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. iIL-17A: inhibidores de la interleucina 17A. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>La estimación puntual varía ampliamente entre los estudios, sin explicación por el análisis de subgrupos. Se utilizó un modelo de efectos aleatorios.

##### 4.1.3.2. DLQI (12-24 semanas): secukinumab, ixekizumab.

|  |           |                    |                    |             |             |         |     |     |   |  |              |               |
|--|-----------|--------------------|--------------------|-------------|-------------|---------|-----|-----|---|--|--------------|---------------|
| 1 RS <sup>(10)</sup><br>(4 brazos [2 ECA]) | MA de ECA | Serio <sup>a</sup> | Serio <sup>a</sup> | No es serio | No es serio | Ninguno | 687 | 690 | - | Diferencia medias<br><b>4,79 menos</b><br>(6,81 menos a 2,77<br>menos) | ⊕⊕⊖⊖<br>Baja | NO IMPORTANTE |
|--|-----------|--------------------|--------------------|-------------|-------------|---------|-----|-----|---|--|--------------|---------------|

DLQI: *Dermatology Life Quality Index*. ECA: ensayos clínicos aleatorizados. iIL-17A: inhibidores de la interleucina 17A. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad de los resultados no explicada.

##### 4.1.3.3. Enfermedad inflamatoria intestinal: número de brotes en pacientes con EII conocida (mediana de 16 semanas): secukinumab, ixekizumab.

|                                 |           |                    |                    |             |             |         |                |              |                                  |   |              |         |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|----------------------------------|---|--------------|---------|
| 1 RS <sup>(11)</sup><br>(7 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | No es serio | Ninguno | 1/2076 (0.05%) | 0/984 (0.0%) | <b>OR* 0.47</b><br>(0.03 a 8.96) | 0 menos por 1000<br>(de 0 menos a 0<br>menos) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|----------------------------------|---|--------------|---------|

##### 4.1.3.4. Enfermedad inflamatoria intestinal: número de nuevos brotes en pacientes con EII no conocida (mediana de 16 semanas): secukinumab, ixekizumab.

|                                 |           |                    |                    |             |             |         |                |              |                                   |   |              |         |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|-----------------------------------|---|--------------|---------|
| 1 RS <sup>(11)</sup><br>(7 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | No es serio | Ninguno | 5/2076 (0.24%) | 0/984 (0.0%) | <b>OR* 1.91</b><br>(0.33 a 11.00) | 0 menos por 1000<br>(de 0 menos a 0<br>menos) | ⊕⊕⊖⊖<br>Baja | CRÍTICA |
|---------------------------------|-----------|--------------------|--------------------|-------------|-------------|---------|----------------|--------------|-----------------------------------|---|--------------|---------|

ECA: ensayo clínico aleatorizado. iIL-17: inhibidores de la interleucina 17. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup> Heterogeneidad entre los estudios y la metodología. El grupo de pacientes con espondiloartritis está integrado por espondilitis anquilosante, espondiloartritis axial no radiográfica y espondiloartritis periférica. \* Método de Peto.

#### 4.1.4. Comparación iLL-17A/17F versus placebo

##### 4.1.4.1. Respuesta PASI 75 (media 14,67 semanas): bimekinumab.

| Evaluación de certeza          |                   |                    |                |                     |             |                       | Nº de pacientes    |                | Efecto                   |   | Certeza | Importancia |            |
|--------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|--------------------|----------------|--------------------------|---|---------|-------------|------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Bimekizumab        | Placebo        | Relativo (95% CI)        | Absoluto (95% CI)                           |         |             |            |
| 1 RS <sup>(8)</sup><br>(3 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 351/447<br>(78.5%) | 29/256 (11.3%) | RR 6.97<br>(4.92 a 9.87) | 676 más por 1000<br>(de 444 más a 1000 más) | ⊕⊕⊕⊖    | Moderada    | IMPORTANTE |

##### 4.1.4.2. Respuesta PASI 100 (media 14,67 semanas): bimekinumab.

|                                |           |                    |             |             |             |         |                    |              |                            |  |      |          |            |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|--------------|----------------------------|--|------|----------|------------|
| 1 RS <sup>(8)</sup><br>(3 ECA) | MA de ECA | Serio <sup>a</sup> | No es serio | No es serio | No es serio | Ninguno | 229/447<br>(51.2%) | 9/256 (3.5%) | RR 14.22<br>(7.47 a 27.06) | 465 más por 1000<br>(de 227 más a 916 más) | ⊕⊕⊕⊖ | Moderada | IMPORTANTE |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|--------------|----------------------------|--|------|----------|------------|

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. PASI 100: Mejoría del 100% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios y exclusivamente estudios en lengua inglesa.

#### 4.1.5. Comparación iLL-17A versus iTNF (adalimumab)

##### 4.1.5.1. Respuesta PASI 100 en pacientes con ≥3% de afectación basal de la superficie corporal (12 a 52 semanas): secukinumab, ixekizumab.

| Evaluación de certeza          |                   |                    |                |                     |             |                       | Nº de pacientes    |                    | Efecto                   |  | Certeza | Importancia |            |
|--------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|--------------------|--------------------|--------------------------|--|---------|-------------|------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | iLL-17             | iTNF               | Relativo (95% CI)        | Absoluto (95% CI)                          |         |             |            |
| 1 RS <sup>(6)</sup><br>(3 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 307/630<br>(48.7%) | 164/553<br>(29.7%) | RR 1.71<br>(1.47 a 1.99) | 211 más por 1000<br>(de 139 más a 294 más) | ⊕⊕⊕⊖    | Moderada    | IMPORTANTE |

##### 4.1.5.2. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (12 a 24 semanas): secukinumab, ixekizumab.

|                                |           |                    |                    |             |                    |         |                    |                    |                          |  |      |          |            |
|--------------------------------|-----------|--------------------|--------------------|-------------|--------------------|---------|--------------------|--------------------|--------------------------|--|------|----------|------------|
| 1 RS <sup>(6)</sup><br>(2 ECA) | MA de ECA | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio | Serio <sup>c</sup> | Ninguno | 323/415<br>(77.8%) | 218/351<br>(62.1%) | RR 1.30<br>(1.17 a 1.43) | 186 más por 1000<br>(de 106 más a 267 más) | ⊕⊖⊖⊖ | Muy baja | IMPORTANTE |
|--------------------------------|-----------|--------------------|--------------------|-------------|--------------------|---------|--------------------|--------------------|--------------------------|--|------|----------|------------|

ECA: ensayos clínicos aleatorizados. iLL-17: inhibidores de la interleucina 17. iTNF: inhibidores del factor de necrosis tumoral. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>La estimación puntual varía ampliamente entre los estudios, sin explicación por el análisis de subgrupos. Se utilizó un modelo de efectos aleatorios. <sup>c</sup>Los intervalos de confianza entre los estudios no se superponen o son diferentes.

#### 4.1.6. Comparación iIL-17 versus controla

##### 4.1.6.1. Eventos adversos: EI (12 a 52 semanas): secukinumab, ixekizumab, bimekizumab, brodalumab.

| Evaluación de certeza                        |                   |                    |                |                     |             |                       | Nº de pacientes |                      | Efecto                    |  | Certeza          | Importancia |
|--|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|----------------------|---------------------------|--|------------------|-------------|
| Nº de estudios                               | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-17          | Control <sup>a</sup> | Relativo (IC95%)          | Absoluto (IC95%)                           |                  |             |
| 1 RS <sup>(12)</sup><br>(5 ECA) <sup>b</sup> | MA de ECA         | Serio <sup>c</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 7/2024 (0.3%)   | 0/1322 (0.0%)        | RR 3.54<br>(0.62 a 20.09) | 0 menos por 1000<br>(de 0 menos a 0 menos) | ⊕⊕⊕⊖<br>Moderada | CRÍTICA     |

ECA: ensayo clínico aleatorizado. EI: enfermedad inflamatoria intestinal. IC: intervalo de confianza. iIL-17: inhibidores de la interleucina 17. MA: metaanálisis. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup> No se especifica si el control es placebo y/o adalimumab. <sup>b</sup> Recogido en 5 de los 11 ECA de la RS. <sup>c</sup> Alto riesgo de sesgo por probable no inclusión de otros estudios.

#### 4.1.7. Comparación iIL-12/23 versus placebo

##### 4.1.7.1. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (rango 12 a 24 semanas): ustekinumab.

| Evaluación de certeza          |                   |                    |                |                     |             |                       | Nº de pacientes    |                | Efecto                   |  | Certeza          | Importancia |
|--------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|--------------------|----------------|--------------------------|--|------------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Ustekinumab        | Placebo        | Relativo (95% CI)        | Absolute (95% CI)                          |                  |             |
| 1 RS <sup>(6)</sup><br>(2 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 222/370<br>(60.0%) | 19/176 (10.8%) | RR 5.56<br>(3.61 a 8.58) | 492 más por 1000<br>(de 282 más a 818 más) | ⊕⊕⊕⊖<br>Moderada | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios.

##### 4.1.7.2. DLQI (12-24 semanas) (ustekinumab).

| Nº de estudios                             | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | Nº de pacientes | Efecto | Certeza | Importancia  |                  |               |
|--|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|-----------------|--------|---------|--|------------------|---------------|
| 1 RS <sup>(10)</sup><br>(4 brazos [2 ECA]) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 471             | 472    | -       | Diferencia medias<br>5,39 menos<br>(6,15 menos a 4,63 menos) | ⊕⊕⊕⊖<br>Moderada | NO IMPORTANTE |

DLQI: *Dermatology Life Quality Index*. ECA: ensayos clínicos aleatorizados. MA: metaanálisis. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios.

#### 4.1.8. Comparación iIL-12/23 (ustekinumab) versus iTNF (adalimumab)

##### 4.1.8.1. Respuesta PASI 100 (24 semanas).

| Evaluación de certeza          |                   |                    |                    |                     |                    |                       | Nº de pacientes |              | Efecto                   |   | Certeza          | Importancia |
|--------------------------------|-------------------|--------------------|--------------------|---------------------|--------------------|-----------------------|-----------------|--------------|--------------------------|---|------------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia     | Evidencia indirecta | Imprecisión        | Otras consideraciones | Ustekinumab     | Adalimumab   | Relativo (95% CI)        | Absoluto (95% CI)                         |                  |             |
| 1 RS <sup>(6)</sup><br>(1 ECA) | MA de ECA         | Serio <sup>a</sup> | Serio <sup>b</sup> | No es serio         | Serio <sup>c</sup> | Ninguno               | 14/23 (60.9%)   | 7/24 (29.2%) | RR 2.09<br>(1.03 a 4.22) | 318 más por 1000<br>(de 9 más a 939 más ) | ⊕⊕⊕⊖<br>Muy baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 100: mejoría del 100% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>No se pudo valorar la consistencia. <sup>c</sup>El intervalo de confianza es amplio. El tamaño muestral es pequeño.

#### 4.1.9. Comparación iIL-23 versus placebo

##### 4.1.9.1. Respuesta PASI 90 (24 semanas): guselkumb, risankizumab, tildrakizumab.

| Evaluación de certeza          |                   |                    |                |                     |             |                       | Nº de pacientes     |                | Efecto                   |  | Certeza          | Importancia          |
|--------------------------------|-------------------|--------------------|----------------|---------------------|-------------|-----------------------|---------------------|----------------|--------------------------|--|------------------|----------------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones | iIL-23              | Placebo        | Relativo (95% CI)        | Absoluto (95% CI)                          |                  |                      |
| 1 RS <sup>(7)</sup><br>(6 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | No es serio | Ninguno               | 661/1491<br>(44.3%) | 94/1335 (7.0%) | RR 6.11<br>(4.99 a 7.49) | 360 más por 1000<br>(de 281 más a 457 más) | ⊕⊕⊕⊖<br>Moderada | CRÍTICA <sup>b</sup> |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 90: Mejoría del 90% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>La variable crítica es PASI 90 a las 12-16 y 48-52 semanas, no a las 24 semanas.

#### 4.1.10. Comparación Abatacept versus placebo

##### 4.1.10.1. Respuesta PASI 75 (24 semanas):

| Evaluación de certeza          |                   |                        |                |                     |                    |                       | Nº de pacientes |             | Efecto                   |  | Certeza          | Importancia |
|--------------------------------|-------------------|------------------------|----------------|---------------------|--------------------|-----------------------|-----------------|-------------|--------------------------|--|------------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo        | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | Abatacept       | Placebo     | Relativo (95% CI)        | Absoluto (95% CI)                          |                  |             |
| 1 RS <sup>(6)</sup><br>(1 ECA) | MA de ECA         | Muy serio <sup>a</sup> | No es serio    | No es serio         | Serio <sup>b</sup> | Ninguno               | 15/84 (17.9%)   | 8/81 (9.9%) | RR 1.81<br>(0.81 a 4.03) | 80 más por 1000<br>(de 19 menos a 299 más) | ⊕⊕⊕⊖<br>Muy baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Muy alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>El intervalo de confianza cruza el 1.

## 4.2. FAME SINTÉTICOS DE DIANA ESPECÍFICOS

### 4.2.1. Comparación Apremilast versus placebo

#### 4.2.1.1. Respuesta PASI 75 (16 semanas):

| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo        | Evaluación de certeza |                     |             |                       | Nº de pacientes |               | Efecto                   |  | Certeza      | Importancia |
|--------------------------------|-------------------|------------------------|-----------------------|---------------------|-------------|-----------------------|-----------------|---------------|--------------------------|--|--------------|-------------|
|                                |                   |                        | Inconsistencia        | Evidencia indirecta | Imprecisión | Otras consideraciones | Apremilast      | Placebo       | Relativo (95% CI)        | Absoluto (95% CI)                        |              |             |
| 1 RS <sup>(6)</sup><br>(1 ECA) | MA de ECA         | Muy serio <sup>a</sup> | No es serio           | No es serio         | No es serio | Ninguno               | 46/213 (21.6%)  | 10/93 (10.8%) | RR 2.01<br>(1.06 a 3.81) | 109 más por 1000<br>(de 6 más a 302 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Muy alto riesgo de sesgo por probable no inclusión de otros estudios.

### 4.2.2. Comparación iJAK versus placebo

#### 4.2.2.1. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (16 semanas): tofacitinib, upadacitinib.

|                                |           |                    |             |             |             |         |                    |                     |                          |  |                  |            |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|---------------------|--------------------------|--|------------------|------------|
| 1 RS <sup>(9)</sup><br>(4 ECA) | MA de ECA | Serio <sup>a</sup> | No es serio | No es serio | No es serio | Ninguno | 525/998<br>(52.6%) | 180/1020<br>(17.6%) | RR 2.96<br>(2.56 a 3.42) | 346 más por 1000<br>(de 275 más a 427 más) | ⊕⊕⊕⊖<br>Moderada | IMPORTANTE |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|---------------------|--------------------------|--|------------------|------------|

ECA: ensayos clínicos aleatorizados. iJAK: inhibidores de la Janus quinasa. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>iJAK: inhibidores de la Janus quinasa (tofacitinib 2 ECA, upadacitinib 2 ECA).

#### 4.2.2.2. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (12 semanas): tofacitinib.

|                                |           |                        |             |             |             |         |                |               |                          |  |              |            |
|--------------------------------|-----------|------------------------|-------------|-------------|-------------|---------|----------------|---------------|--------------------------|--|--------------|------------|
| 1 RS <sup>(6)</sup><br>(1 ECA) | MA de ECA | Muy serio <sup>a</sup> | No es serio | No es serio | No es serio | Ninguno | 66/152 (43.4%) | 12/82 (14.6%) | RR 2.97<br>(1.71 a 5.16) | 288 más por 1000<br>(de 104 más a 609 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|--------------------------------|-----------|------------------------|-------------|-------------|-------------|---------|----------------|---------------|--------------------------|--|--------------|------------|

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Muy alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Intervalo de confianza contiene el 1.

#### 4.2.2.3. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (16 semanas): tofacitinib 5 mg dos veces al día.

|                                |           |                    |             |             |                    |         |                |                |                          |   |              |            |
|--------------------------------|-----------|--------------------|-------------|-------------|--------------------|---------|----------------|----------------|--------------------------|---|--------------|------------|
| 1 RS <sup>(9)</sup><br>(2 ECA) | MA de ECA | Serio <sup>a</sup> | No es serio | No es serio | Serio <sup>b</sup> | Ninguno | 52/162 (30.1%) | 24/168 (14.3%) | RR 2.16<br>(1.14 a 4.07) | 166 más por 1000<br>(de 20 más a 439 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE |
|--------------------------------|-----------|--------------------|-------------|-------------|--------------------|---------|----------------|----------------|--------------------------|---|--------------|------------|

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Heterogeneidad moderada entre los estudios ( $I^2 = 51\%$ ).

#### 4.2.2.4. Respuesta PASI 75 en pacientes con ≥3% de afectación basal de la superficie corporal (16 semanas): upadacitinib 15 mg al día.

|                                |           |                    |             |             |             |         |                    |                |                          |  |                  |            |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|----------------|--------------------------|--|------------------|------------|
| 1 RS <sup>(9)</sup><br>(2 ECA) | MA de ECA | Serio <sup>a</sup> | No es serio | No es serio | No es serio | Ninguno | 202/344<br>(58.7%) | 66/342 (19.3%) | RR 3.03<br>(2.40 a 3.83) | 392 más por 1000<br>(de 270 más a 546 más) | ⊕⊕⊕⊖<br>Moderada | IMPORTANTE |
|--------------------------------|-----------|--------------------|-------------|-------------|-------------|---------|--------------------|----------------|--------------------------|--|------------------|------------|

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.  
<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios.

#### 4.2.3. Comparación iJAK (tofacitinib) versus iTNF (adalimumab).

##### 4.2.3.1. Respuesta PASI 75 (12 semanas):

| Evaluación de certeza          |                   |                    |                |                     |                    |                       | Nº de pacientes |               | Efecto                   |  | Certeza      | Importancia |
|--------------------------------|-------------------|--------------------|----------------|---------------------|--------------------|-----------------------|-----------------|---------------|--------------------------|--|--------------|-------------|
| Nº de estudios                 | Diseño de estudio | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones | Tofacitinib     | Adalimumab    | Relativo (95% CI)        | Absolute (95% CI)                          |              |             |
| 1 RS <sup>(6)</sup><br>(1 ECA) | MA de ECA         | Serio <sup>a</sup> | No es serio    | No es serio         | Serio <sup>b</sup> | Ninguno               | 66/152 (43.4%)  | 30/77 (39.0%) | RR 1.11<br>(0.80 a 1.56) | 43 más por 1000<br>(de 78 menos a 218 más) | ⊕⊕⊖⊖<br>Baja | IMPORTANTE  |

ECA: ensayos clínicos aleatorizados. MA: metaanálisis. PASI: *psoriasis area and severity index*. PASI 75: Mejoría del 75% del PASI. RR: riesgo relativo. RS: revisión sistemática.

<sup>a</sup>Alto riesgo de sesgo por probable no inclusión de otros estudios. <sup>b</sup>Intervalo de confianza contiene el 1.

## Obesity and smoking

### Clinical question

In PsA, do obesity and/or smoking increase disease activity, accelerate radiographic progression of structural damage and impair treatment response?

Pregunta: Fumador vs. No fumador.

| Nº de estudios   | Diseño de estudio                  | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión        | Otras consideraciones  | Número de pacientes              |                                  | Efecto  |   | Certeza          | Importancia |
|--|------------------------------------|-----------------|----------------|---------------------|--------------------|--|----------------------------------|----------------------------------|---|---|------------------|-------------|
|  |                                    |                 |                |                     |                    |  | Fumadores                        | No fumadores                     | Relativo (IC 95%)   | Absoluto (IC 95%)   |                  |             |
| <b>Índice SvH</b>  |                                    |                 |                |                     |                    |  |                                  |                                  |   |   |                  |             |
| 1  | Estudio observacional <sup>1</sup> | No serio        | NA             | No serio            | No serio           | Ajustan por factores de confusión. Escaso tiempo de seguimiento.       | FUTURE 1 n=104<br>FUTURE 5 n=176 | FUTURE 1 n=435<br>FUTURE 5 n=750 |   | <u>Progresión anual</u><br><br>-0,03<br>(IC 95% -0,37 a 0,31) | ⊕⊕○○<br>Baja     | CRÍTICA     |
| <b>Supervivencia del fármaco</b>                           |                                    |                 |                |                     |                    |  |                                  |                                  |   |   |                  |             |
| <b>Varios FAMEb (anti-TNF, anti-IL12/IL23 y anti-IL17)</b> |                                    |                 |                |                     |                    |  |                                  |                                  |   |   |                  |             |
| 1  | Estudio observacional <sup>2</sup> | No serio        | NA             | No serio            | No serio           | Ajustan por factores de confusión.<br>Tamaño muestral grande (n=2.301) | 373                              | 1.928                            | Supervivencia a los 5 años:<br><b>HR 1,11</b><br>(IC 95% 1,0 a 1,2); p>0,05.                |   | ⊕⊕○○<br>Baja     | IMPORTANTE  |
| <b>Anti-TNF (infliximab, etanercept, adalimumab)</b>       |                                    |                 |                |                     |                    |  |                                  |                                  |   |   |                  |             |
| 1  | Estudio observacional <sup>3</sup> | No serio        | NA             | No serio            | Serio <sup>a</sup> | Ajustan por factores de confusión.                                     | 33                               | 69                               | <u>Adherencia al tratamiento:</u><br>Fumadores:<br><b>HR 1,56</b> (IC 95% 0,97 a 2,15] años |   | ⊕○○○<br>Muy baja | IMPORTANTE  |

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|  |  |  |  |  |  |  |  |  | <ul style="list-style-type: none"> <li>- infliximab <b>HR:</b><br/><b>1,62</b> (IC 95% 1,06 a<br/>2,48)</li> <li>- etanercept <b>HR:</b><br/><b>1,74</b> (IC 95% 1,14 a<br/>2,66)</li> <li>- adalimumab <b>HR:</b><br/><b>0,80</b> (IC 95% 0,52 a<br/>1,23).</li> </ul> <p><u>Discontinuación de</u><br/><u>tratamiento</u> <b>HR:</b><br/><b>1,52</b><br/>[IC 95% 1,08 a<br/>1,13].</p> |  |  |  |
|--|--|--|--|--|--|--|--|--|--|--|--|--|

Referencias: 1. Luttringer, 2021. 2. Haddad 2021. 3. Soubrier 2016.

a. Pequeño tamaño muestral y periodo de seguimiento corto. En algunos casos también IC95% que cruza la línea del no efecto.

Pregunta: Sobrepeso vs. normopeso.

| Evaluación de certeza            |   |                 |                |                     |             |                                    | Nº de pacientes        |                        | Efecto  |   | Certeza      | Importancia |
|----------------------------------|---|-----------------|----------------|---------------------|-------------|------------------------------------|------------------------|------------------------|---|---|--------------|-------------|
| Nº de estudios                   | Diseño de estudio                                     | Riesgo de sesgo | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones              | Sobrepeso              | Normopeso              | Relativo (IC 95%)   | Absoluto (IC 95%)   |              |             |
| <b>NAT y NAD</b>                 |   |                 |                |                     |             |                                    |                        |                        |   |   |              |             |
| 1                                | Estudio observacional <sup>1</sup>                    | No serio        | NA             | No serio            | No serio    | Ajustan por factores de confusión. | 285                    | 306                    |   | <b>NAT media (DE)</b><br><u>Sobrepeso:</u> 5,78 (7,17)<br><u>Normopeso:</u> 4,7 (5,31)<br>p=0,05<br><br><b>NAD media (DE)</b><br><u>Sobrepeso:</u> 9,18 (10,36)<br><u>Normopeso:</u> 8,2 (9,23)<br>p=0,25 | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>Índice SvH</b>                |   |                 |                |                     |             |                                    |                        |                        |   |   |              |             |
| 1                                | Estudio observacional <sup>2</sup>                    | No serio        | NA             | No serio            | No serio    | Tiempo de seguimiento corto        | ABA: 75<br><br>PBO: 55 | ABA: 29<br><br>PBO: 34 | Con ABA:<br><b>OR 1,15</b><br>(IC 95% 0,5 a 2,68);<br>p=0,739<br><br>Con PBO:<br><b>OR 1,22</b><br>(IC 95% 0,5 a 2,9);<br>p=0,660 |   | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>Supervivencia del fármaco</b> |   |                 |                |                     |             |                                    |                        |                        |   |   |              |             |
| <b>Anti-TNF</b>                  |   |                 |                |                     |             |                                    |                        |                        |   |   |              |             |
| 1                                | RS <sup>3</sup> (estudio observacional <sup>4</sup> ) | No serio        | NA             | No serio            | No serio    | Ajustan por factores de confusión. | No hay datos           | No hay datos           | <b>OR 0,91</b><br>(IC 95% 0,5-1,68);<br>p=0,773   |   | ⊕⊕○○<br>Baja | IMPORTANTE  |

Referencias: 1. Vallejo-Yagüe 2022. 2. Mc Innes 2019. 3. Gialouri 2023. 4. Chiricozzi 2016.

Pregunta: Obesidad vs. normopeso.

| Evaluación de certeza            |   |                    |                |                     |             |                                    | Nº de pacientes      |                    | Efecto  |   | Certeza      | Importancia |
|----------------------------------|---|--------------------|----------------|---------------------|-------------|------------------------------------|----------------------|--------------------|---|---|--------------|-------------|
| Nº de estudios                   | Diseño de estudio                                     | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones              | Obesidad             | Normopeso          | Relativo (IC 95%)   | Absoluto (IC 95%)   |              |             |
| <b>NAT y NAD</b>                 |   |                    |                |                     |             |                                    |                      |                    |   |   |              |             |
| 1                                | Estudio observacional <sup>1</sup>                    | No serio           | NA             | No serio            | No serio    | Ajustan por factores de confusión. | 183                  | 306                |   | <b>NAT media (DE)</b><br><u>Obesidad</u> : 4,88 (5,34)<br><u>Normopeso</u> : 4,7 (5,31)<br>p=0,73 | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>Índice SvH</b>                |   |                    |                |                     |             |                                    |                      |                    |   |   |              |             |
| 1                                | Estudio observacional <sup>2</sup>                    | No serio           | NA             | No serio            | No serio    | Tiempo de seguimiento corto        | ABA: 101<br>PBO: 112 | ABA: 29<br>PBO: 34 | Con ABA: <b>OR 0,87</b><br>(IC 95% 0,38 a 1,96);<br>p=0,728   | Con PBO: <b>OR 1,17</b><br>(IC 95% 0,54 a 2,56);<br>p=0,694                                       | ⊕⊕○○<br>Baja | CRÍTICA     |
| <b>Supervivencia del fármaco</b> |   |                    |                |                     |             |                                    |                      |                    |   |   |              |             |
| <b>Anti-TNF</b>                  |   |                    |                |                     |             |                                    |                      |                    |   |   |              |             |
| 1                                | RS <sup>3</sup> (estudio observacional <sup>4</sup> ) | No serio           | NA             | No serio            | No serio    | Ajustan por factores de confusión  | ND                   | ND                 | <b>OR 0,53</b><br>(IC 95% 0,22 a 1,23);<br>p=0,136  | ⊕⊕○○<br>Baja  | IMPORTANTE   |             |
| <b>Anti-IL12/IL23</b>            |   |                    |                |                     |             |                                    |                      |                    |   |   |              |             |
| 1                                | RS <sup>3</sup> (estudio observacional <sup>5</sup> ) | Serio <sup>a</sup> | NA             | No serio            | NA          | Ajustan por factores de confusión. | ND                   | ND                 | La obesidad a nivel basal no se asoció al riesgo de interrupción de ustekinumab tras 12 meses de seguimiento. | ⊕○○○<br>Muy baja  | IMPORTANTE   |             |

Varios FAMEb (anti-TNF, anti-IL12/IL23 y anti-IL17)

|   |   |          |    |          |          |   |    |    |   |  |              |            |
|---|---|----------|----|----------|----------|---|----|----|---|--|--------------|------------|
| 1 | RS <sup>3</sup> (estudio observacional <sup>b</sup> ) | No serio | NA | No serio | No serio | Ajustan por factores de confusión.<br>Tamaño muestral grande (n=2.301). | ND | ND | Supervivencia a los 5 años:<br><b>HR 1,126</b><br>(IC 95% 0,99 a 1,28);<br>p>0,05 |  | ⊕⊕○○<br>Baja | IMPORTANTE |
|---|---|----------|----|----------|----------|---|----|----|---|--|--------------|------------|

Referencias: 1. Vallejo-Yagüe 2022. 2. Mc Innes 2019. 3. Gialouri 2023. 4. Chiricozzi 2016. 5. Iannone 2018. 6. Haddad 2021.

a. Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.

Pregunta: Obesidad vs. no obesidad.

| Evaluación de certeza            |   |                    |                |                     |             |                                    | Nº de pacientes |             | Efecto  |                   | Certeza          | Importancia |
|----------------------------------|---|--------------------|----------------|---------------------|-------------|------------------------------------|-----------------|-------------|---|-------------------|------------------|-------------|
| Nº de estudios                   | Diseño de estudio                                     | Riesgo de sesgo    | Inconsistencia | Evidencia indirecta | Imprecisión | Otras consideraciones              | Obesidad        | No obesidad | Relativo (IC 95%)   | Absoluto (IC 95%) |                  |             |
| <b>NAD y NAT</b>                 |   |                    |                |                     |             |                                    |                 |             |   |                   |                  |             |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio           | NA             | No serio            | No serio    | No se aportan datos.               | ND              | ND          | No hay diferencias significativas en cuanto al cambio en el recuento de NAD entre basal y 3 o 6 meses de seguimiento en pacientes que inician un primer anti-TNF. |                   | ⊕⊕○○<br>Baja     | CRÍTICO     |
| <b>Supervivencia del fármaco</b> |   |                    |                |                     |             |                                    |                 |             |   |                   |                  |             |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>2</sup> ) | No serio           | NA             | No serio            | No serio    | Ajustan por factores de confusión. | ND              | ND          | HR 1,64<br>(IC 95% 1,32 a 2,03)   |                   | ⊕⊕○○<br>Baja     | IMPORTANTE  |
| <b>Anti-IL12/IL23</b>            |   |                    |                |                     |             |                                    |                 |             |   |                   |                  |             |
| 1                                | RS <sup>1</sup> (estudio observacional <sup>3</sup> ) | Serio <sup>a</sup> | NA             | No serio            | No serio    | Tamaño muestral pequeño (n=58).    | ND              | ND          | La obesidad a nivel basal se asoció a una mayor tasa de interrupción de ustekinumab tras 12 meses de seguimiento (63,6% vs 13,9%, p=0,0001).                      |                   | ⊕○○○<br>Muy baja | IMPORTANTE  |

Referencias: 1. Gialouri 2023. 2. Højgaard 2016. 3. Almirall 2017.

a. Evaluación de la calidad mediante la Escala Newcastle Ottawa 2010 realizada por los autores de la RS con resultado de riesgo de sesgo intermedio.

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