Targeted Immune Modulators for Plaque Psoriasis, Psoriatic Arthritis, and Generalized Pustular Psoriasis: Update

Systematic Review

Washington P&T Committee Meeting

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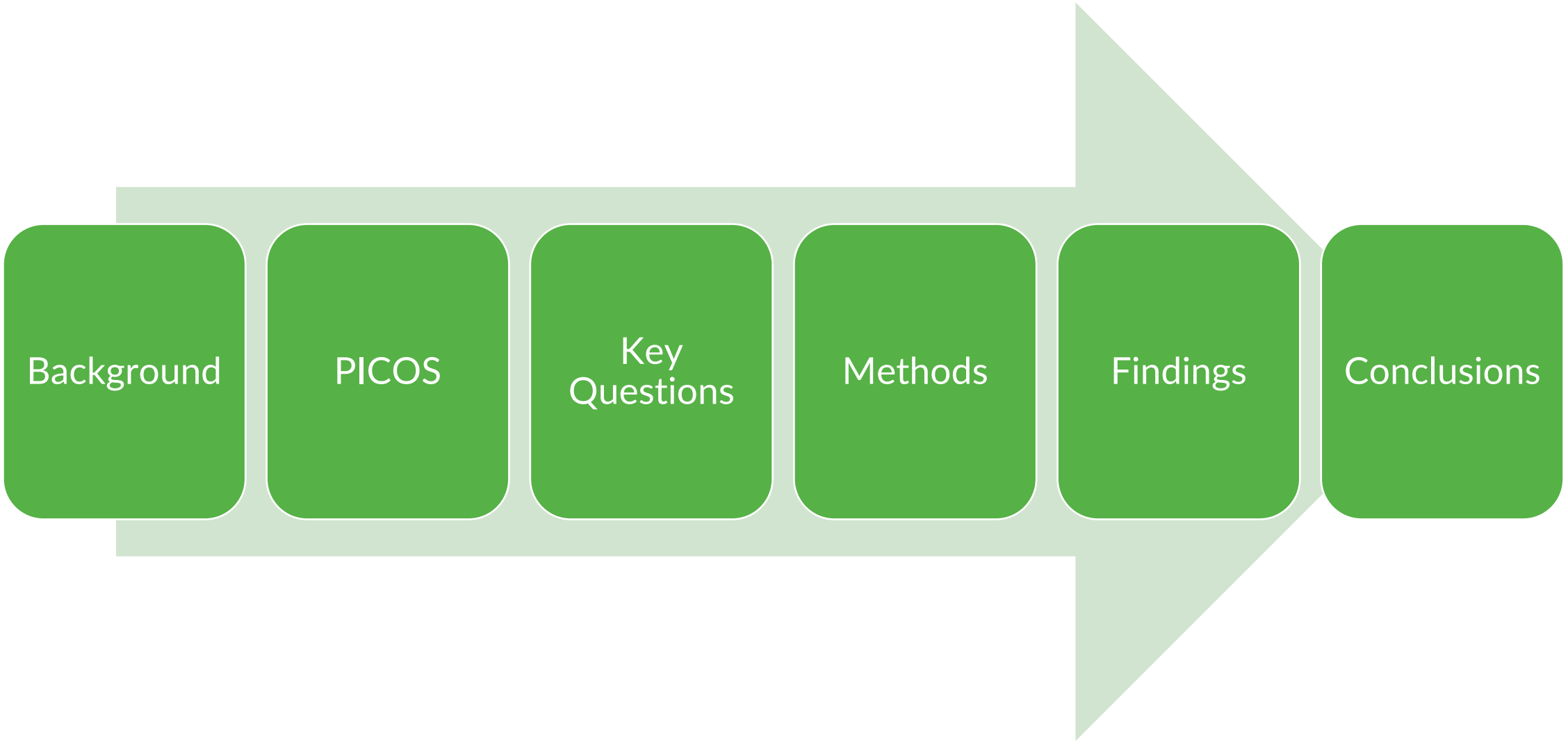
Overview


Background
PICOS
Key Questions
Methods
Findings
Conclusions

Background

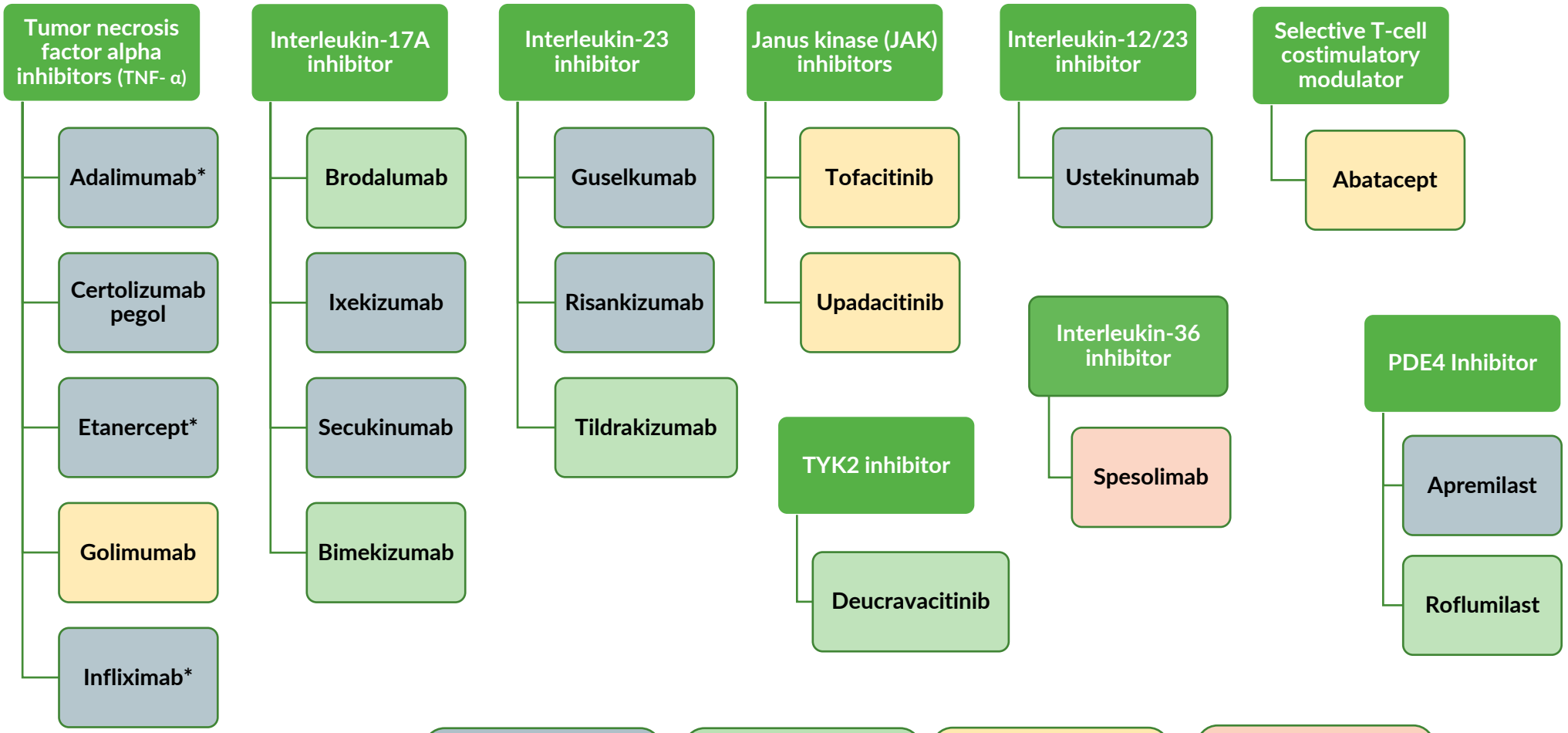
Abbreviations Used

- AE: adverse event
- ARD: absolute risk difference
- CI: confidence interval
- GRADE: certainty of evidence
- HR: hazard ratio
- IRR: incident rate ratio
- KQ: key question
- QoL: quality of life
- RCT: randomized controlled trial
- RoB: risk of bias
- RR: risk ratio
- SAE: serious adverse event
- SF-36 PCS: 36-item short form health survey, physical health component score
- SF-36 MCS: 36-item short form health survey, mental health component score
- SPARCC: Spondylarthritis Consortium of Canada
- TIM: targeted immune modulator

Background

- **Plaque psoriasis** is a chronic inflammatory disease that affects the skin, scalp, and nails; erythrosquamous scaling skin lesions are hallmark
- **Psoriatic arthritis** is a chronic inflammatory arthritis associated with psoriasis
- **Generalized pustular psoriasis** is characterized by eruption of pustules
- **Targeted immune modulators (TIMs)** are biologic drugs used to treat plaque psoriasis and psoriatic arthritis by selectively blocking mechanisms involved in the inflammatory and immune responses
  - First TIM for psoriasis (alefacept) FDA-approved in 2003
  - First TIM for psoriatic arthritis (etanercept) FDA-approved in 2002
  - First TIM for generalized pustular psoriasis (spesolimab) FDA approved in 2022
  - Additional agents (including biosimilars) have since been approved

TIMs for Plaque Psoriasis, Psoriatic Arthritis, and Generalized Pustular Psoriasis



**indicates biosimilars are available*

PICOS (for Updated Systematic Review)

Population	Adult outpatients with plaque psoriasis, psoriatic arthritis, or generalized pustular psoriasis
Interventions	FDA-approved TIMs and respective biosimilars or pipeline drugs for the treatment of plaque psoriasis, psoriatic arthritis, or generalized pustular psoriasis
Comparators	• FDA-approved drugs: head-to-head comparisons • Pipeline drugs: any listed TIM, standard of care, placebo
Outcomes	Measures of clinical improvement and disease remission, quality of life, adverse events, serious adverse events, and other health outcomes
Study Designs	Randomized controlled trials ≥ 12 weeks duration

Change in criteria from last report: Removal of cohort studies, addition of generalized pustular psoriasis (GPP)

Key Questions

1. Comparative effectiveness of TIMs
2. Comparative harms of TIMs
3. Variation by subgroups
4. Characteristics of ongoing studies

Methods

Methods

- PubMed, Cochrane Library
  August 1, 2021 through August 1, 2023 (with active surveillance through November 30, 2023)
- Individual study risk-of-bias assessment
- OpenEpi for RR and CI calculations
- Grading of Recommendations, Assessments, Development and Evaluation (GRADE) approach for overall certainty of evidence
- ClinicalTrials.gov searches for ongoing studies

Abbreviations. CI: confidence intervals; RR: risk ratio.

DERP Risk of Bias Assessment

- **Low**

  Clear reporting of methods and mitigation of potential biases and conflicts of interest

- **Moderate**

  Incomplete information about methods that might mask important limitations or a meaningful conflict of interest

- **High**

  Clear flaws that might introduce serious bias

GRADE Certainty of Evidence

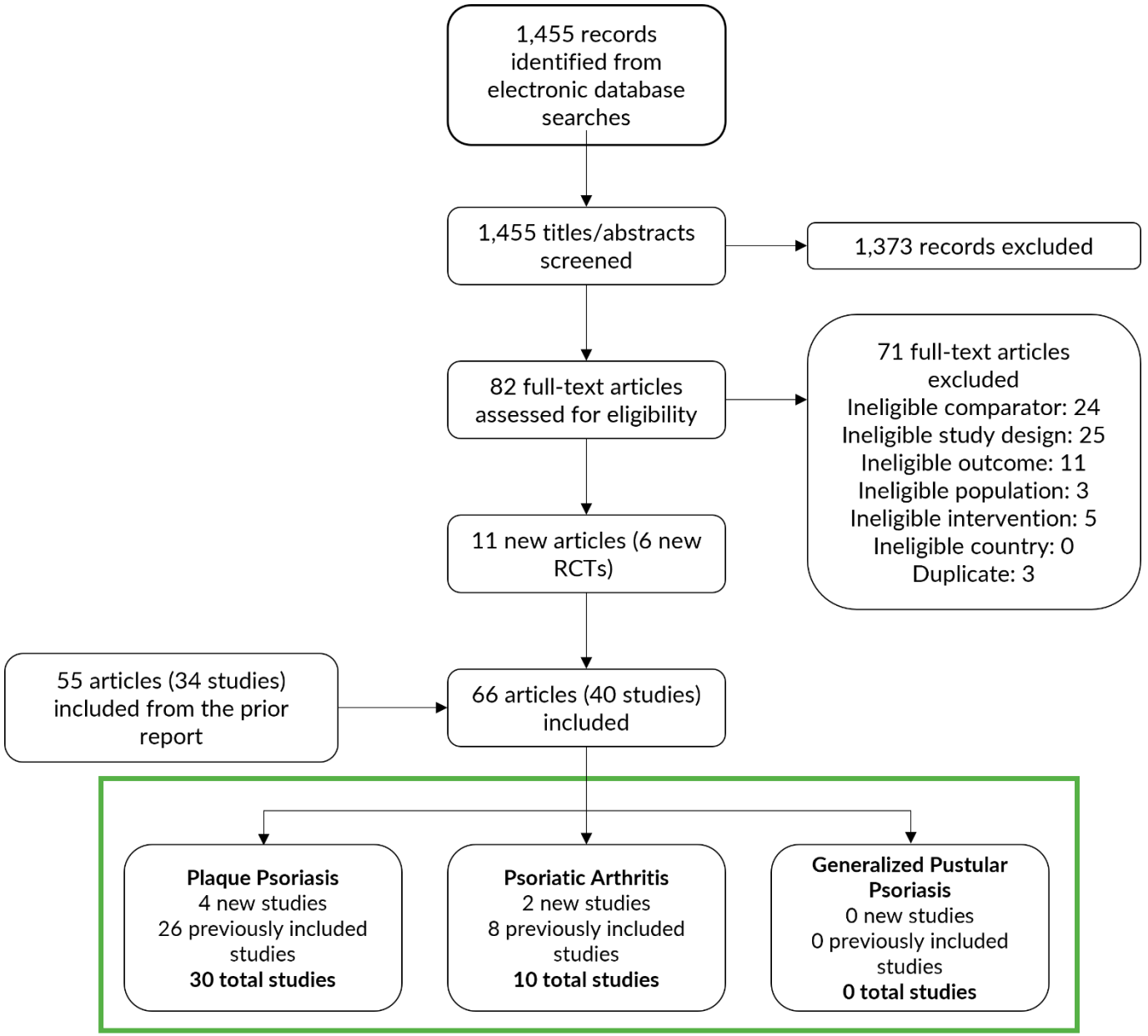
Outcomes Rated: *Disease remission, clinical improvement, QoL, AEs, SAEs*

- **High** *(RCTs start here)*
  Very confident that the estimate of effect of intervention on outcome lies close to the true effect
- **Moderate**
  Moderately confident in estimate of effect of intervention on outcome; true effect is likely close to estimate, but possibly different
- **Low**
  Little confidence in estimate of effect of intervention on outcome; true effect may be substantially different from estimate
- **Very Low**
  No confidence in estimate of effect of intervention on outcome; true effect is likely substantially different from estimate

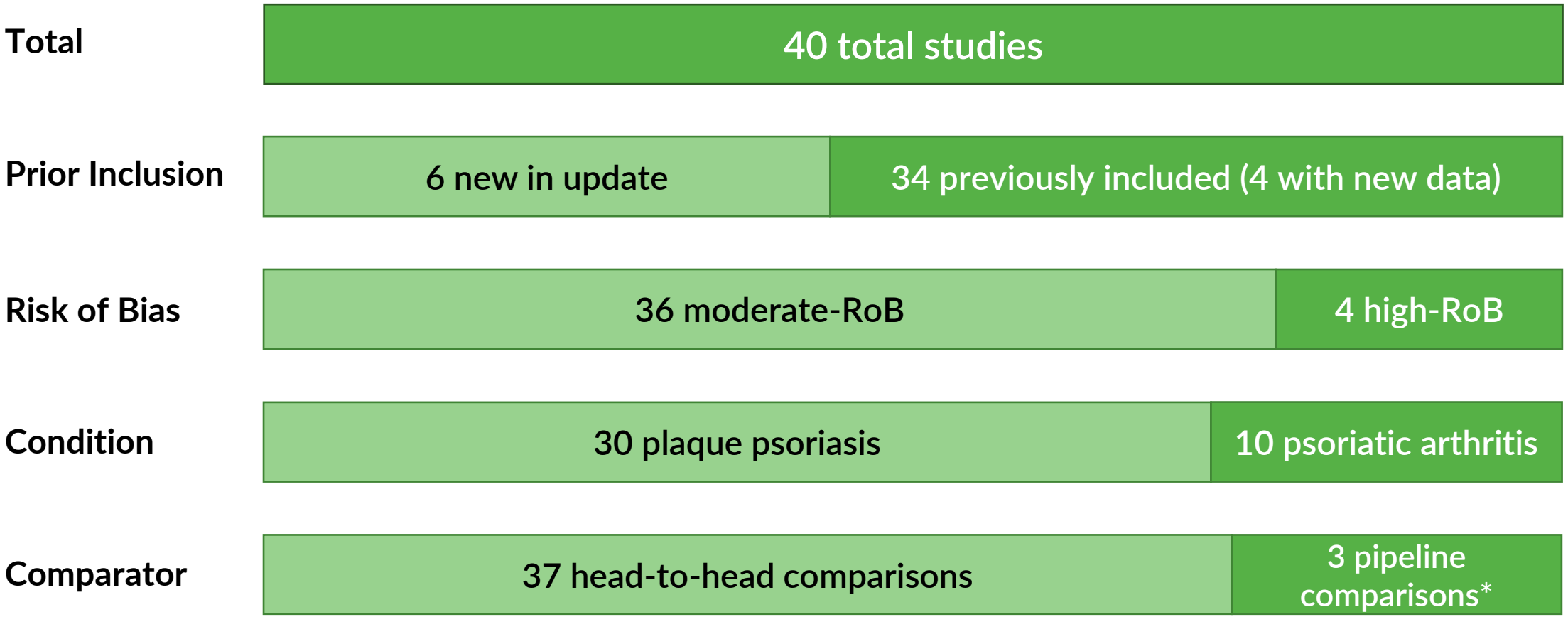
Findings

Literature Yield and Study Characteristics

Study Flow Diagram



Findings: Study Characteristics



*Note. * denotes some are placebo-controlled and some are head-to-head comparisons. Abbreviation.*
Abbreviation. RoB: risk of bias.

Structure of Findings

- Plaque psoriasis
- Psoriatic arthritis
- ~~Generalized pustular psoriasis~~: ***no findings***

- *For each condition:*
  - Comparative benefits from RCTs (KQ1)
    - Variation in outcomes by subgroup (KQ3)
  - Comparative harms from RCTs (KQ2)
  - Comparative benefits and harms from pipeline drugs (KQ1, KQ2)

Outcomes Used

- **ACR:** American College of Rheumatology Response (ACR20, ACR50, ACR70, representing 20%, 50%, and 70% reduction in score, respectively)
- **DLQI:** Dermatology Life Quality Index (0 or 1 = no impact on QoL)
- **PASI:** Psoriasis Area and Severity Index (PASI 50, 75, 90, 100, representing 50%, 75%, 90%, and 100% reduction in score from baseline, respectively)
- **PGA/IGA/PtGA:** Physician/Investigator/Patient Global Assessment (0 or 1 = disease remission)

Findings

Comparative Effectiveness from RCTs in Plaque Psoriasis

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KQ1: Comparative Effectiveness in Plaque Psoriasis
Overview of Comparisons Identified

Moderate-RoB study

High-RoB study

	Adalimumab	Apremilast	Certolizumab pegol	Guselkumab	Infliximab	Ixekizumab	Secukinumab	Tildrakizumab	Tofacitinib	Ustekinumab
Adalimumab				**3 RCTs**						
Bimekizumab	1 RCT						1 RCT			1 RCT
Brodalumab										2 RCTs
Deucravacitinib		**2 RCTs**								
Etanercept		1 RCT	1 RCT		1 RCT	2 RCTs	1 RCT	1 RCT	1 RCT	1 RCT
Ixekizumab				1 RCT			1 RCT			1 RCT
Risankizumab	1 RCT	**1 RCT**					**1 RCT**			3 RCTs
Secukinumab				1 RCT	**1 RCT**					2 RCTs

Note. Bolded cells with yellow text and green outline have new studies or new data

KQ1: Comparative Effectiveness in Plaque Psoriasis

Apremilast vs. etanercept (1 RCT, N = 166)

- **Clinical improvement; GRADE: Low**
  - No difference (PASI 75) at 16 weeks
- **QoL; GRADE: Low**
  - No difference (change in DLQI) at 16 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

Bimekizumab vs. adalimumab (1 RCT, N = 478)

- **Disease remission; GRADE: Moderate**
  - Bimekizumab more effective (PASI 90: 86.2% vs. 47.2%) at 16 weeks
- **QoL; GRADE: Moderate**
  - Bimekizumab more effective (DLQI 0 or 1: 67.1% vs. 47.8%) at 24 weeks

Bimekizumab vs. secukinumab (1 RCT, N = 743)

- **Disease remission; GRADE: Moderate**
  - Bimekizumab more effective (PASI 100: 61.7% vs. 48.9%) at 16 weeks
- **QoL; GRADE: Moderate**
  - Bimekizumab more effective (DLQI 0 or 1: 77.7% vs. 70.3%) at 48 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

Bimekizumab vs. ustekinumab (1 RCT, N = 484)

- **Disease remission; GRADE: Moderate**
  - Bimekizumab more effective (PASI 90: 85% vs. 60%) at 16 weeks
- **QoL; GRADE: Moderate**
  - Bimekizumab more effective (DLQI 0 or 1: 75% vs. 63%) at 52 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

Brodalumab vs. ustekinumab (2 RCTs, N = 3,712)

- **Disease remission; GRADE: High**
  - Brodalumab more effective (PASI 100: ARDs, 18 and 22 percentage points) at 12 weeks and 52 weeks
- **QoL; GRADE: High**
  - Brodalumab more effective (DLQI 0/1: ARDs, 14 and 15 percentage points) at 12 weeks and 52 weeks

Certolizumab vs. etanercept (1 RCT, N = 502)

- **Clinical improvement; GRADE: Moderate**
  - Certolizumab 400 mg more effective (PASI 75: RR 1.2; 95% CI, 1.04 to 1.5) at 12 weeks
  - No difference for 200-mg dosage

The FDA approved dosage for certolizumab is an initial dose of 400 mg followed by 400-mg maintenance doses, or 200-mg maintenance doses for people weighing less than 90 kg.

KQ1: Comparative Effectiveness in Plaque Psoriasis

New studies

Deucravacitinib vs. apremilast (2 RCTs, N = 1,265)

- **Clinical improvement; GRADE: High**
  - Deucravacitinib more effective (PASI 75: RR, 1.7; 95% CI, 1.3 to 2.1 and RR, 1.3; 95% CI, 1.1 to 1.6) at 16 weeks
- **QoL; GRADE: High**
  - Deucravacitinib was more effective than apremilast for achieving DLQI 0 or 1 at 16 weeks (RR, 1.4; 95% CI, 1.1 to 1.9 and RR, 1.6; 95% CI, 1.3 to 2.1) and at 24 weeks (RR, 2.0; 95% CI, 1.5 to 2.7 and RR, 1.9; 95% CI, 1.5 to 2.5)

KQ1: Comparative Effectiveness in Plaque Psoriasis

Etanercept vs. infliximab (1 RCT, N = 50)

- **Disease remission; GRADE: Very low**
  - Etanercept less effective (PASI 75: 35% vs. 72%) at 24 weeks
- **QoL; GRADE: Very low**
  - No difference (relative change in SF-36 PCS and MCS)

Etanercept vs. ixekizumab (2 RCTs, N = 2,570)

- **Disease remission; GRADE: High**
  - Etanercept less effective (PASI 75: ARDs, 31 and 48 percentage points) at 12 weeks
- **QoL; GRADE: High**
  - Etanercept less effective (DLQI 0 or 1: ARDs, 20 or 30 percentage points)

KQ1: Comparative Effectiveness in Plaque Psoriasis

Etanercept vs. secukinumab (1 RCT, N = 1,306)

- **Disease remission; GRADE: High**
  - Etanercept less effective (PASI 75: 44% vs. 77% [secukinumab 300 mg] vs. 67% [secukinumab 150 mg]) at 12 weeks
- **QoL; GRADE: Moderate**
  - Etanercept less effective (change in DLQI: 7.9 points [etanercept] vs. 10.4 points [secukinumab 300 mg] vs. 9.7 points [secukinumab 150 mg]) at 12 weeks

Both the 150-mg and 300-mg dosages of secukinumab are FDA-approved.

KQ1: Comparative Effectiveness in Plaque Psoriasis

Etanercept vs. tildrakizumab (1 RCT, N=1,090)

- **Disease remission; GRADE: High**
  - Etanercept less effective (PASI 75: 48% vs. 66% [tildrakizumab 200 mg] vs. 61% [tildrakizumab 100 mg]) at 12 weeks and (PASI 75: 54% vs. 73% [both 200- and 100-mg dosages]) at 28 weeks
- **QoL; GRADE: Moderate**
  - Etanercept less effective (DLQI 0 or 1: 36% vs. 47% [tildrakizumab 200 mg] vs. 40% [tildrakizumab 100 mg] at 12 weeks and at 28 weeks
- **Subgroup analyses based on metabolic syndrome status**
  - No difference in effectiveness based on having metabolic syndrome (or not having it)

The FDA-approved dose for tildrakizumab is 100 mg at weeks 0 and 4, then every 12 weeks.

KQ1: Comparative Effectiveness in Plaque Psoriasis

Etanercept vs. tofacitinib (1 RCT, N = 1,106)

- **Disease remission; GRADE: Moderate**
  - Etanercept more effective (PASI 75: 59% vs. 40%) at 12 weeks than tofacitinib 5-mg dosage, but no different than tofacitinib 10-mg dosage
- **Clinical improvement; GRADE: Moderate**
  - Etanercept more effective (PASI 50: 80% vs. 66%) at 12 weeks than tofacitinib 5-mg dosage, but no different than tofacitinib 10-mg dosage
- **QoL; GRADE: Low (10 mg), Moderate (5 mg)**
  - Etanercept more effective (DLQI change ≥ 5 points: 75% vs. 66%) at 12 weeks than tofacitinib 5-mg dosage, but no different than 10-mg dosage

Tofacitinib is only FDA-approved for psoriatic arthritis at a dosage of 5 mg twice daily.

KQ1: Comparative Effectiveness in Plaque Psoriasis

Etanercept vs. ustekinumab (1 RCT, N = 903)

- **Disease remission; GRADE: Low**
  - Etanercept less effective (PASI 75: 57% vs. 68% [ustekinumab 45 mg] vs. 74% [ustekinumab 90 mg]) at 12 weeks

New data

Guselkumab vs. adalimumab (3 RCTs, N = 1,658)

- **Disease remission; GRADE: High**
  - Guselkumab more effective (PGA 0 or 1: ARDs, 16 to 28 percentage points) at 16 weeks
- **QoL; GRADE: Moderate**
  - Guselkumab more effective (DLQI 0 or 1: ARDs, 13 to 15 percentage points*; mean change, −0.6 to −1.7 points) at 16 weeks

*Note. * denotes only statistically significant in 1 of the 2 trials reporting this measure.*

KQ1: Comparative Effectiveness in Plaque Psoriasis

New study

Guselkumab vs. secukinumab (2 RCTs, N = 1,088)

- **Disease remission; GRADE: Moderate**
  - Guselkumab more effective (PASI 90: 84% vs. 70%) at 48 weeks (primary endpoint)
  - Guselkumab noninferior (PASI 75: 85% vs. 80%) at combined 12-week and 48-week endpoints
  - Guselkumab with a lower response (PASI 90: 69% vs 76%; no statistical testing) at 12 weeks only
- **Subgroup analyses**
  - Guselkumab remained superior across all subgroups at 28 weeks based on age, weight, BMI, severity of disease, body area affected, and prior medication use evaluated.
- **Clinical Improvement; GRADE: Very low**
  - Guselkumab less effective for clinical improvement in a single treatment-refractory plaque (TCS of 0, 1, or 2: 40% vs. 60% P = .17) at 16 weeks

Study population: PASI score lower than 10 at baseline but ≥1 plaque refractory to treatment with ustekinumab

KQ1: Comparative Effectiveness in Plaque Psoriasis

Ixekizumab vs. guselkumab (1 RCT, N = 1,027)

- **Disease remission; GRADE: Moderate**
  - Ixekizumab more effective (PASI 100: RR, 1.7) at 12 weeks, no difference at 24 weeks (RR, 0.96)
- **QoL; GRADE: Moderate**
  - Ixekizumab more effective (DLQI 0 or 1, actual values NR) at 12 weeks, but no difference at 24 weeks

Ixekizumab vs. secukinumab (1 RCT, N = 54)

- **Disease remission; GRADE: Moderate**
  - No difference (sPGA) at 24 weeks
- **Clinical improvement; GRADE: Moderate**
  - No difference (Genital Psoriasis Severity Score) at 24 weeks

Study population all had genital psoriasis

KQ1: Comparative Effectiveness in Plaque Psoriasis

Ixekizumab vs. ustekinumab (1 RCT, N=302)

- **Disease remission; GRADE: Moderate**
  - Ixekizumab more effective (PASI 90: 73% vs. 42%) at 12 weeks and continued to be superior at 24 and 52 weeks
- **QoL; GRADE: Moderate**
  - Ixekizumab more effective (DLQI 0 or 1: 61% vs. 45%) at 12 weeks, continued to be superior at 24 and 52 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

Risankizumab vs. adalimumab (1 RCT, N = 605)

- **Disease remission; GRADE: Moderate**
  - Risankizumab more effective (PASI 90: 72% vs. 47%) at 16 weeks
- **QoL; GRADE: Moderate**
  - Risankizumab more effective (DLQI 0 or 1: 66% vs. 49%) at 16 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

New study

Risankizumab vs. apremilast (1 RCT, N = 352)

- **Disease remission; GRADE: Moderate**
  - Risankizumab more effective (PASI 90: 55.9% vs. 5.1%) at 16 weeks
- **Clinical improvement; GRADE: Moderate**
  - Risankizumab more effective (PASI 75: 84.7% vs. 18.8%) at 16 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

New data

Risankizumab vs. secukinumab (1 RCT, N = 327)

- **Disease remission; GRADE: Moderate**
  - Risankizumab more effective (PASI 90: ARD, 8.2 percentage points) at 16 weeks and at 52 weeks (PASI 90: ARD, 29.8 percentage points)
- **Subgroup analyses: no significant difference in any outcomes**
  - Age < 40 years vs. ≥ 40 years, male vs. female, White vs. non-White, BMI < 25 vs. 25 to 30 vs. ≥ 30, disease severity at baseline, prior biologic use vs. no use, presence vs. absence of psoriatic arthritis, current vs. former vs. never smoker, and disease duration < 15 years vs. ≥ 15 years)

KQ1: Comparative Effectiveness in Plaque Psoriasis

Risankizumab vs. ustekinumab (3 RCTs, N = 1,065)

- **Disease remission; GRADE: High**
  - Risankizumab more effective (PASI 90: ARDs, 28 to 37 percentage points) at 12 to 16 weeks, similar findings at 52 weeks
- **QoL; GRADE: High**
  - Risankizumab more effective (DLQI 0 or 1: ARDs, 19 to 23 percentage points) at 12 to 16 weeks
  - Risankizumab more effective (% achieving minimally clinically important difference on EQ-5D-5L: 44% vs. 32%) at 52 weeks

KQ1: Comparative Effectiveness in Plaque Psoriasis

Secukinumab vs. ustekinumab (2 RCTs, N = 1,778)

- **Disease remission; GRADE: High**
  - Secukinumab more effective (PASI 90: ARDs, 21 and 23 percentage points) at 16 weeks, similar findings in PASI 100 at 52 weeks (PASI 90: ARDs, 14 and 13 percentage points)
- **QoL; GRADE: High**
  - Secukinumab more effective (DLQI 0 or 1: ARDs, 12 and 15 percentage points) at 16 weeks and at 52 weeks (DLQO 0 or 1: ARDs, 12 and 8 percentage points)

Findings

Comparative Harms in Plaque Psoriasis

KQ2: Comparative Harms in Plaque Psoriasis

- All RCTs included for KQ1 (comparative effectiveness) also reported comparative harms
- The focus of the next few slides is on the comparisons from RCTs where a significant difference in AE or SAE was found and the certainty of evidence is at least *Low*

KQ2: Comparative Harms in Plaque Psoriasis

Apremilast vs. etanercept (1 RCT, N = 166)

- **Adverse events; GRADE: Low**
  - Lower incidence for apremilast (RR, 0.75; 95% CI, 0.58 to 0.95)

KQ2: Comparative Harms in Plaque Psoriasis

Etanercept vs. tildrakizumab (1 RCT, N = 1,090)

- **Adverse events; GRADE: Moderate**
  - Higher incidence for etanercept vs. tildrakizumab 100-mg dosage during weeks 1 to 12 (RR, 1.2; 95% CI, 1.0 to 1.4) and during weeks 13 to 28 (RR, 1.2; 95% CI, 1.1 to 1.5)
  - Higher incidence for etanercept vs. tildrakizumab 200-mg dosage during weeks 13 to 28 only (RR, 1.3; 95% CI, 1.1 to 1.5)

KQ2: Comparative Harms in Plaque Psoriasis

New study

Risankizumab vs. apremilast (1 RCT, N = 352)

- **Adverse events; GRADE: Moderate**
  - Lower incidence for risankizumab (RR, 0.68; 95% CI, 0.54 to 0.86)

KQ2: Comparative Harms in Plaque Psoriasis

Risankizumab vs. ustekinumab (3 RCTs, N = 1,065)

- **Adverse events; GRADE: Low**
  - Lower incidence for risankizumab during weeks 17 to 52 in 1 study (RR, 0.75; 95% CI, 0.64 to 0.87); no significant differences in the other 2 studies
- **SAEs; GRADE: Low**
  - Lower incidence for risankizumab during weeks 1 to 16 in 1 study (RR, 0.29; 95% CI, 0.11 to 0.77); no significant differences in the other 2 studies

Findings

Summary of Evidence for TIMs for Plaque Psoriasis

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Treatments for Plaque Psoriasis: Summary, Part 1

Comparison	Clinical Improvement	Disease Remission	Quality of Life	Overall AEs	SAEs
Apremilast vs. etanercept (1 RCT)	●●○○		●●○○	●●○○	●○○○
Bimekizumab vs. adalimumab (1 RCT)		●●●○	●●●○	●●●○	●●○○
Bimekizumab vs. secukinumab (1 RCT)		●●●○	●●●○	●●●○	●●○○
Bimekizumab vs. ustekinumab (1 RCT)		●●●○	●●●○	●●●○	●●○○
Brodalumab vs. ustekinumab (2 RCTs)		●●●●	●●●●	●●●○	●○○○
Certolizumab pegol[a] vs. etanercept (1 RCT)	●●●○			●●●○	●○○○
Deucravacitinib vs. apremilast (2 RCTs)[b]	●●●●		●●●●	●●●●	●○○○

*Color key: **purple** indicates no difference; **blue** favors first TIM listed; **red** favors second TIM listed; **gray** indicates inability to determine direction of effect; **bolded blue** comparisons represent new studies or data for this update.*

Notes [a] Only higher dose, no difference with lower dose. [b] New comparison in this update. [c] New RCT in this update for a previously included comparison. [d] Ixekizumab was more effective at 12 weeks but showed no differences at 24 weeks. [e] No difference in disease remission at 16 weeks but risankizumab was more effective at 52 weeks. [f] Inconsistent findings across 3 studies; no differences in 1 study; some differences in other studies but only for specific time periods.

GRADE certainty of evidence: No evidence *(blank)*; Very Low ●○○○; Low ●●○○; Moderate ●●●○; High ●●●●

Treatments for Plaque Psoriasis: Summary, Part 2

Comparison	Clinical Improvement	Disease Remission	Quality of Life	Overall AEs	SAEs
Etanercept vs. infliximab (1 RCT)	●○○○		●○○○	●○○○	●○○○
Etanercept vs. ixekizumab (2 RCTs)	●●●●	●●●●	●●●●	●●●○	●●○○
Etanercept vs. secukinumab (1 RCT)	●●●●	●●●●	●●●○	●●●○	●●○○
Etanercept vs. tildrakizumab (1 RCT)	●●●●		●●●○	●●●○	●●○○
Etanercept vs. tofacitinib (1 RCT)	●●●○ **vs. lower dosage**	●●●○ **vs. lower dosage**	●●○○ **vs. lower dosage**	●●○○	●●○○
Etanercept vs. ustekinumab (1 RCT)	●●●○			●●○○	●●○○

*Color key: **purple** indicates no difference; **blue** favors first TIM listed; **red** favors second TIM listed; **gray** indicates inability to determine direction of effect.*

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GRADE certainty of evidence: No evidence *(blank)*; Very Low ●○○○; Low ●●○○; Moderate ●●●○; High ●●●●

Treatments for Plaque Psoriasis: Summary, Part 3

Comparison	Clinical Improvement	Disease Remission	Quality of Life	Overall AEs	SAEs
Guselkumab vs. adalimumab (3 RCTs)		●●●●	●●●○	●●○○	●●○○
Guselkumab vs. secukinumab (2 RCTs)[c]	●●●○	●●●○		●●○○	●●○○
Ixekizumab vs. guselkumab (1 RCT)		●●●●[d]	●●●●[d]	●●●●	●●○○
Ixekizumab vs. secukinumab (1 RCT)	●●○○	●●○○		●●○○	●○○○
Ixekizumab vs. ustekinumab (1 RCT)		●●●○	●●●○	●●○○	●●○○
Risankizumab vs. adalimumab (1 RCT)		●●●○	●●●○	●●○○	●●○○
Risankizumab vs. apremilast (1 RCT)[b]	●●●○	●●●○		●●●○	●●○○
Risankizumab vs. secukinumab (1 RCT)		●●●○[e]		●●●○	●●○○
Risankizumab vs. ustekinumab (3 RCTs)		●●●●	●●●●	●●○○[f]	●●○○
Secukinumab vs. ustekinumab (2 RCTs)		●●●●	●●●●	●●●○	●●○○

*Color key: **purple** indicates no difference; **blue** favors first TIM listed; **red** favors second TIM listed; **gray** indicates inability to determine direction of effect; **bolded blue** comparisons represent new studies or data for this update.*

Notes [a] Only higher dose, no difference with lower dose. [b] New comparison in this update. [c] New RCT in this update for a previously included comparison. [d] Ixekizumab was more effective at 12 weeks but showed no differences at 24 weeks. [e] No difference in disease remission at 16 weeks but risankizumab was more effective at 52 weeks. [f] Inconsistent findings across 3 studies; no differences in 1 study; some differences in other studies but only for specific time periods.

GRADE certainty of evidence: No evidence *(blank)*; Very Low ●○○○; Low ●●○○; Moderate ●●●○; High ●●●●

Pipeline Treatments for Plaque Psoriasis

- We found no eligible studies of pipeline agents for plaque psoriasis

Findings

Comparative Effectiveness in Psoriatic Arthritis

KQ1: Comparative Effectiveness in Psoriatic Arthritis

Overview of Comparisons Identified

	Etanercept or Infliximab	Ixekizumab	Secukinumab	Tofacitinib	Upadacitinib	TNF-α Inhibitors
Adalimumab	1 RCT	**2 RCTs**	1 RCT	1 RCT	**1 RCT**	
Ustekinumab						1 RCT

Moderate-RoB study

High-RoB study

Note. Bolded cells with yellow text and green outline have new studies or new data

KQ1: Comparative Effectiveness in Psoriatic Arthritis

Adalimumab vs. etanercept vs. infliximab (1 RCT, N = 100)

- **Clinical improvement; GRADE: Very low**
  - ACR20 response at 1 year (70% vs. 72% vs. 75%, no statistical significance testing)

KQ1: Comparative Effectiveness in Psoriatic Arthritis

Adalimumab vs. tofacitinib (1 RCT, N = 422)

- **Clinical improvement; GRADE: Low**
  - ACR20 response at 1 year: 60% (adalimumab) vs. 70% (tofacitinib 10 mg) vs. 68% (tofacitinib 5 mg); no statistical testing
- **Skin disease remission; GRADE: Low**
  - PASI 75 response at 1 year: 56% (adalimumab) vs. 67% (tofacitinib 10 mg) vs. 56% (tofacitinib 5 mg); no statistical testing
- **QoL; GRADE: Low**
  - Change in SF-36 PCS: 6.2 (adalimumab) vs. 5.7 (tofacitinib 10 mg) vs. 5.5 (tofacitinib 5 mg); no statistical testing

The FDA-approved dosage of tofacitinib is 5 mg twice daily.

KQ1: Comparative Effectiveness in Psoriatic Arthritis

New data

Ixekizumab vs. adalimumab (2 RCTs, N = 983)

- **Clinical improvement; GRADE: Moderate**
  - ACR 20 (joint disease) at 24 weeks: 62% (ixekizumab every 2 weeks) vs. 58% (ixekizumab every 4 weeks) vs. 57% (adalimumab) in first study (no statistical significance testing); RR, 0.96; 95% CI, 0.86 to 1 in a second study
  - PASI 75 (skin disease) at 24 weeks: 80% (ixekizumab every 2 weeks) vs. 71% (ixekizumab every 4 weeks) vs. 54% (adalimumab) in first study (no statistical significance testing); RR, 1.2; 95% CI, 1.06 to 1.30 in a second study
- **Clinical improvement; GRADE: High**
  - ACR 50 and PASI 100 (composite joint and skin): 36% (ixekizumab) vs. 28% (adalimumab); RR, 1.3; 95% CI, 1.01 to 1.6 at 24 weeks and 39% (ixekizumab) vs. 26% (adalimumab); RR, 1.5; 95% CI, 1.8 to 1.9 at 52 weeks (1 study; high certainty of evidence)
  - PASI 75 response at 52 weeks: RR, 1.1; 95% CI, 1.04 to 1.3 (1 study; high certainty of evidence)
- **New subgroup data:** ixekizumab more effective in people with comorbid plaque psoriasis and psoriatic arthritis

The FDA-approved dosage for ixekizumab is 160 mg at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12; then 80 mg every 4 weeks.

KQ1: Comparative Effectiveness in Psoriatic Arthritis

Secukinumab vs. adalimumab (1 RCT, N = 853)

- **Clinical improvement; GRADE: Moderate**
  - ACR20: no difference at 52 weeks
- **Skin disease remission; GRADE: Moderate**
  - Secukinumab more effective (PASI 90: RR, 1.5; 95% CI, 1.3 to 1.7)

KQ1: Comparative Effectiveness in Psoriatic Arthritis

New data

Upadacitinib vs. adalimumab (1 RCT, N = 1,281)

- **Clinical improvement; GRADE: Moderate**
  - ACR 20
    - Upadacitinib 30 mg more effective at 12 weeks (RR, 1.2; 95% CI, 1.1 to 1.3) and 56 weeks (RR, 1.1; 95% CI, 1.001 to 1.2) and no difference with 15-mg dosage
- **QoL; GRADE: Moderate**
  - Change in HAQ-DI
    - Upadacitinib 15 mg and 30 mg dosage more effective at 12 weeks (difference in mean change, −0.08; 95% CI, −0.15 to −0.01 for 15 mg; and −0.14; 95% CI, −0.20 to −0.07 for 30 mg)
    - Upadacitinib 30-mg dosage more effective at 56 weeks (RR, 1.2; 95% CI, 1.01 to 1.3) for percent with ≥ 0.35 change in score and no difference with 15-mg dosage

The FDA-approved dosage of upadacitinib is 15 mg daily.

KQ1: Comparative Effectiveness in Psoriatic Arthritis

Ustekinumab vs. TNF-α inhibitors (1 RCT, N = 47)

- **Disease remission; GRADE: Very low**
  - Ustekinumab more effective for enthesitis remission (SPARCC enthesitis index: 74% vs. 42%) at 24 weeks
  - Ustekinumab more effective for skin disease remission (PASI 90: 86% vs. 29%) at 24 weeks
  - No difference in arthritis remission (tender joint count, swollen joint count) at 24 weeks
- **QoL; GRADE: Very low**
  - Ustekinumab more effective as measured by SF-36 PCS, but no difference as measured by SF-36 MCS

Findings

Comparative Harms in Psoriatic Arthritis

KQ2: Comparative Harms in Psoriatic Arthritis

- 6 of the 7 RCTs included for KQ1 also reported comparative harms for KQ2
- The focus of the next few slides is on the comparisons from RCTs where a significant difference in AEs or SAEs was found and the certainty of evidence is at least *Low*

KQ2: Comparative Harms in Psoriatic Arthritis

New data

Upadacitinib vs. adalimumab (1 RCT, N = 1,281)

- **Adverse events; GRADE: Moderate**
  - Higher incidence with upadacitinib 30-mg dosage (RR, 1.1; 95% CI, 1.02 to 1.2) at 12 weeks and at 56 weeks (RR, 1.3; 95% CI, 1.1 to 1.5); no difference with the 15-mg dosage at 12 or 56 weeks

Findings

Summary of Evidence for TIMs for Psoriatic Arthritis

OHSU

TIMs for Psoriatic Arthritis

Comparisons	Clinical Improvement	Disease Remission	Quality of Life	Overall AEs	SAEs
Adalimumab vs. etanercept and infliximab (1 RCT)	●○○○ arthritis			●○○○	
Adalimumab vs. tofacitinib (1 RCT)	●●○○[a] arthritis	●●○○[a] arthritis	●●○○[b]	●●○○	●○○○
Ixekizumab vs. adalimumab (2 RCTs)	●●●○ arthritis ●●●○ skin			●●○○	●○○○
Secukinumab vs. adalimumab (1 RCT)	●●●○ arthritis	●●●○ skin	●●●○	●●●○	●●○○
Upadacitinib vs. adalimumab (1 RCT)	●●●○[c] arthritis		●●●○	●●●○[d]	●●○○
Ustekinumab vs. TNF-α inhibitors (1 RCT)		●○○○ arthritis; ●○○○ enthesitis & skin	●○○○		

*Color key: **purple** indicates no difference; **blue** favors first TIM listed; **red** favors second TIM listed; **gray** indicates inability to determine direction of effect; **bolded blue** comparisons represent new studies or data for this update.*

Notes: [a] Numerically favors the tofacitinib but no statistical testing was conducted; [b] Numerically favors adalimumab, but no statistical testing was conducted. [C] Only higher dose of upadacitinib favored; no difference with lower dose. [d] No difference with lower dose; adalimumab favored vs. higher dose.

GRADE certainty of evidence: No evidence *(blank)*; Very Low ●○○○; Low ●●○○; Moderate ●●●○; High ●●●●

Pipeline Treatments for Psoriatic Arthritis

- 2 new RCTs
- 1 previously included studies carried forward
  - Bimekizumab compared with placebo

Comparisons	Clinical Improvement	Disease Remission	Quality of Life	Overall AEs	SAEs
Bimekizumab vs. placebo (3 RCTs)[a]	●●●● arthritis		●●●●	●●○○	●○○○
Bimekizumab vs. adalimumab (1 RCT)[a,b]	●●●○ arthritis		●●●○	●●●○	●●○○

*Color key: **purple** indicates no difference; **blue** favors first TIM listed; **red** favors second TIM listed; **gray** indicates inability to determine direction of effect; **bolded blue** comparisons represent new studies or data for this update.*

Notes: [a] New RCT in this update for a previously included comparison. [b] New comparison in this update.

GRADE certainty of evidence: No evidence *(blank)*; Very low ●○○○; Low ●●○○; Moderate ●●●○; High ●●●●

Limitations

- For some comparisons:
  - Direct evidence still lacking
  - Limited long-term efficacy and safety data available
- Manufacturers sponsored nearly all RCTs
- Studies not powered for harm outcomes
- This review did not include:
  - RCTs shorter than 12 weeks
  - Data from conference abstracts or press releases
  - Studies published in languages other than English

Ongoing Studies

Ongoing Studies Summary

- 10 RCTs
  - 2 for plaque psoriasis
  - 8 for psoriatic arthritis
  - 0 for general pustular psoriasis
- Sponsorship
  - Drug manufacturers: 9
  - Academic or university: 1

Conclusions

Conclusions: Plaque Psoriasis

- Largest body of comparative, direct evidence is for etanercept and ustekinumab compared with other TIM agents. For clinical improvement or disease remission outcomes with moderate to high certainty:

Etanercept is less effective than:

Certolizumab pegol (GRADE: *Moderate*)
Ixekizumab (GRADE: *High*)
Secukinumab (GRADE: *High*)
Tildrakizumab (GRADE: *High*)
Ustekinumab (GRADE: *Moderate*)

Ustekinumab is less effective than:

Bimekizumab (GRADE: *Moderate*)
Brodalumab (GRADE: *High*)
Ixekizumab (GRADE: *Moderate*)
Risankizumab (GRADE: *High*)
Secukinumab (GRADE: *High*)

*Color key: **blue font** indicates high certainty, **purple font** indicates moderate certainty.*

Conclusions: Plaque Psoriasis

- Various other TIMs demonstrate superior effectiveness in pairwise comparisons (GRADE: *Moderate to High*)
- Few differences in harms among TIM agents were observed (GRADE: *Very low to Moderate*)

*Color key: **blue font** indicates high certainty; **purple font** indicates moderate certainty; **red font** indicates very low certainty.*

Conclusions: Psoriatic Arthritis

- Limited head-to-head comparisons available
- ***Upadacitinib may be more effective than adalimumab*** for improvement in arthritis and skin disease but has **higher incidence of AEs** (GRADE: *Moderate*)
- ***Ixekizumab and secukinumab are no different than adalimumab*** for improvement in arthritis, but are **more effective** for improving skin disease (GRADE: *Moderate*) with **similar harms** (GRADE: *Very low* to *Moderate*)

Color key: purple font indicates moderate certainty; red font indicates very low certainty.

Questions?

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GRADE: Certainty of Evidence Summary (1 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Apremilast vs. etanercept		
Clinical improvement (1 RCT)	●●○○ (low)	No difference
QoL (1 RCT)	●●○○ (low)	No difference
AEs (1 RCT)	●●○○ (low)	Favors etanercept
SAEs (1 RCT)	●○○○ (very low)	Unable to determine
Bimekizumab[b] vs. adalimumab		
Disease remission (1 RCT)	●●●○ (moderate)	Favors bimekizumab
QoL (1 RCT)	●●●○ (moderate)	Favors bimekizumab
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Bimekizumab[b] vs. secukinumab		
Disease remission (1 RCT)	●●●○ (moderate)	Favors bimekizumab
QoL (1 RCT)	●●●○ (moderate)	Favors bimekizumab
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Bimekizumab[b] vs. ustekinumab		
Disease remission (1 RCT)	●●●○ (moderate)	Favors bimekizumab
QoL (1 RCT)	●●●○ (moderate)	Favors bimekizumab
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference

Notes. [a] For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator. [b] In prior report as pipeline.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (2 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Brodalumab vs. ustekinumab		
Disease remission (2 RCTs)	●●●● (high)	Favors brodalumab
QoL (2 RCTs)	●●●● (high)	Favors brodalumab
AEs (2 RCTs)	●●●○ (moderate)	No difference
SAEs (2 RCTs)	●○○○ (very low)	Unable to determine
Certolizumab vs. with etanercept		
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors higher dose of certolizumab
AE (1 RCT)	●●●○ (moderate)	No difference
SAE (1 RCT)	●○○○ (very low)	Unable to determine
Deucravacitinib vs. apremilast[c]		
Clinical improvement (2 RCTs)	●●●● (high)	Favors deucravacitinib
AE (2 RCTs)	●●●● (high)	No difference
SAE (2 RCTs)	●○○○ (very low)	Unable to determine
Etanercept vs. infliximab		
Clinical improvement (1 RCT)	●○○○ (very low)	Favors infliximab
QoL (1 RCT)	●○○○ (very low)	No difference
AEs (1 RCT)	●○○○ (very low)	No difference
SAEs (1 RCT)	●○○○ (very low)	Unable to determine

Notes. [a] For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator. [c] New comparison in this report.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (3 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Etanercept vs. ixekizumab		
Clinical improvement (2 RCTs)	●●●● (high)	Favors ixekizumab
Disease remission (2 RCTs)	●●●● (high)	Favors ixekizumab
QoL (2 RCTs)	●●●● (high)	Favors ixekizumab
AEs (2 RCTs)	●●●○ (moderate)	No difference
SAEs (2 RCTs)	●●○○ (low)	No difference
Etanercept vs. secukinumab		
Clinical improvement (1 RCT)	●●●● (high)	Favors secukinumab
Disease remission (1 RCT)	●●●● (high)	Favors secukinumab
QoL (1 RCT)	●●●○ (moderate)	Favors secukinumab
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Etanercept vs. tildrakizumab		
Clinical improvement (1 RCT)	●●●● (high)	Favors tildrakizumab
QoL (1 RCT)	●●●○ (moderate)	Favors tildrakizumab
AEs (1 RCT)	●●●○ (moderate)	No difference for higher dose at week 12; favors tildrakizumab for both doses at week 28
SAEs (1 RCT)	●●○○ (low)	No difference
Etanercept vs. tofacitinib (not FDA-approved for plaque psoriasis)		
Disease remission (1 RCT)	●●●○ (moderate)	Lower dose favors etanercept[d]
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors etanercept[d]
QoL (1 RCT)	●●○○ (low)	Favors etanercept[d]
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference

Notes. [a] *For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator.* [d] *For lower dosage of tofacitinib (5 mg), but no difference for higher dosage (10 mg).*
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (4 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Etanercept vs. ustekinumab		
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors ustekinumab
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Guselkumab vs. adalimumab		
Disease remission (3 RCTs)	●●●● (high)	Favors guselkumab
QoL (3 RCTs)	●●●○ (moderate)	Favors guselkumab
AEs (3 RCTs)	●●○○ (low)	No difference
SAEs (3 RCTs)	●●○○ (low)	No difference
Guselkumab vs. secukinumab[e]		
Disease remission (1 RCT)	●●●○ (moderate)	Favors guselkumab[f]
Clinical improvement (1 RCT)	●●●○ (moderate)	No difference
Clinical improvement (1 RCT)-unique population[g]	●○○○ (very low)	No difference
AEs (2 RCTs)	●●○○ (low)	No difference
SAEs (2 RCTs)	●●○○ (low)	No difference
Ixekizumab vs. guselkumab		
Disease remission (1 RCT)	●●●● (high)	Favors ixekizumab at 12 weeks, no difference at 24 weeks
QoL (1 RCT)	●●●● (high)	Favors ixekizumab at 12 weeks, no difference at 24 weeks
AEs (1 RCT)	●●●● (high)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference

Notes. [a] For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator. [e] Data from a new RCT in this report. [f] Favors guselkumab at 48 weeks, favors secukinumab at 12 weeks; [g] Population included people with low PASI score (< 10) but a treatment-refractory plaque after ustekinumab therapy; outcome measure not typical of measures used in other studies.

Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (5 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Ixekizumab vs. secukinumab		
Disease remission (1 RCT)	●●○○ (low)	No difference
Clinical improvement (1 RCT)	●●○○ (low)	No difference
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●○○○ (very low)	Unable to determine
Ixekizumab vs. ustekinumab		
Disease remission (1 RCT)	●●●○ (moderate)	Favors ixekizumab
QoL (1 RCT)	●●●○ (moderate)	Favors ixekizumab
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Risankizumab vs. adalimumab		
Disease remission (1 RCT)	●●●○ (moderate)	Favors risankizumab
QoL (1 RCT)	●●●○ (moderate)	Favors risankizumab
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Risankizumab vs. apremilast[c]		
Disease remission (1 RCT)	●●●○ (moderate)	Favors risankizumab
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors risankizumab
AEs (1 RCT)	●●●○ (moderate)	Favors risankizumab
SAEs (1 RCT)	●●○○ (low)	No difference

Notes. [a] *For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator.* [c] *New comparison in this report.*
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (6 of 6)

Comparative Effectiveness and Harms: Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Risankizumab vs. secukinumab		
Disease remission (1 RCT)	●●●○ (moderate)	No difference at 16 weeks, favors risankizumab at 1 year
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Risankizumab vs. ustekinumab		
Disease remission (3 RCTs)	●●●● (high)	Favors risankizumab
QoL (3 RCTs)	●●●● (high)	Favors risankizumab
AEs (3 RCTs)	●●○○ (low)	No difference
SAEs (3 RCTs)	●●○○ (low)	No difference
Secukinumab vs. ustekinumab		
Disease remission (2 RCTs)	●●●● (high)	Favors secukinumab
QoL (2 RCTs)	●●●● (high)	Favors secukinumab
AEs (2 RCTs)	●●●○ (moderate)	No difference
SAEs (2 RCTs)	●●○○ (low)	No difference

Notes. [a] For efficacy outcomes, "favors" refers to a larger improvement vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (1 of 2)

Comparative Effectiveness and Harms: Psoriatic Arthritis

Outcome	Certainty of Evidence	Relationship[a]
Adalimumab vs. etanercept and infliximab		
Clinical improvement (1 RCT)	●○○○ (very low)	No difference
AEs (1 RCT)	●○○○ (very low)	Favors adalimumab[b]
Adalimumab vs. tofacitinib		
Clinical improvement arthritis (1 RCT)	●●○○ (low)	Favors tofacitinib[c]
Skin disease remission (1 RCT)	●●○○ (low)	Favors tofacitinib[c]
QoL (1 RCT)	●●○○ (low)	Favors adalimumab[d]
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●○○○ (very low)	Unable to determine
Ixekizumab vs. adalimumab[e]		
Clinical improvement—joint (2 RCTs)	●●●○ (moderate)	No difference
Clinical improvement—skin (2 RCTs)	●●●○ (moderate)	Favors ixekizumab
AEs (2 RCTs)	●●○○ (low)	No difference
SAEs (2 RCTs)	●○○○ (very low)	Unable to determine

Notes. [a] For efficacy outcomes, 'favors' refers to a larger improvement compared to the comparator; for harm outcomes, 'favors' refers to a lower incidence of harm relative to the comparator; [b] Adalimumab favored compared with either etanercept of infliximab, infliximab favored compared with etanercept; [c] Favors the 10 mg twice daily dosage but no difference with the 5 mg twice daily dosage; [d] Ixekizumab dose intervals varied between studies and based on severity of diseases but not enough information to draw firm conclusions; some findings only significant for 1 of the dosing intervals; [e] Previously included comparison with new study for this update.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary (2 of 2)

Comparative Effectiveness and Harms: Psoriatic Arthritis

Outcome	Certainty of Evidence	Relationship[a]
Secukinumab vs. adalimumab		
Clinical improvement: arthritis (1 RCT)	●●●○ (moderate)	No difference
Disease remission: skin (1 RCT)	●●●○ (moderate)	Favors secukinumab
QoL (1 RCT)	●●●○ (moderate)	No difference
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Upadacitinib vs. adalimumab		
Clinical improvement—arthritis (1 RCT)	●●●○ (moderate)	Favors upadacitinib (higher dose only)
QoL (1 RCT)	●●●○ (moderate)	Favors upadacitinib
AEs (1 RCT)	●●●○ (moderate)	Favors adalimumab (higher dose only)
SAEs (1 RCT)	●●○○ (low)	No difference
Ustekinumab vs. TNF-α inhibitors[e]		
Disease remission-enthesitis (1 RCT)	●○○○ (very low)	Favors ustekinumab
Disease remission-arthritis (1 RCT)	●○○○ (very low)	No difference
Disease remission-skin (1 RCT)	●○○○ (very low)	Favors ustekinumab
QoL (1 RCT)	●○○○ (very low)	Favors ustekinumab[f]

Notes. [a] For efficacy outcomes, 'favors' refers to a larger improvement compared to the comparator; for harm outcomes, 'favors' refers to a lower incidence of harm relative to the comparator; [e] Previously included comparison with new study for this update; [f] New comparison for this update.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.

GRADE: Certainty of Evidence Summary

Comparative Effectiveness and Harms: Psoriatic Arthritis (Pipeline Agents)

Outcome	Certainty of Evidence	Relationship[a]
Bimekizumab vs. adalimumab		
Clinical improvement (1 RCT)	●●●○ (moderate)	No difference
QoL (1 RCT)	●●●○ (moderate)	No difference
AEs (1 RCT)	●●●○ (moderate)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference
Bimekizumab vs. placebo[b]		
Clinical improvement (1 RCT)	●●●● (high)	Favors bimekizumab
QoL (3 RCTs)	●●●● (high)	Favors bimekizumab
AEs (3 RCTs)	●●○○ (low)	Favors placebo
SAEs (3 RCTs)	●○○○ (very low)	Unable to determine

Notes. [a] *For efficacy outcomes, 'favors' refers to a larger improvement compared to the comparator; for harm outcomes, 'favors' refers to a lower incidence of harm relative to the comparator;* [b] *New comparison for this update.*
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event.


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