Targeted Immune Modulators for Plaque Psoriasis and Psoriatic Arthritis: Update

Systematic Review

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Executive Summary

Background

Targeted immune modulators (TIMs) are a category of medications used to treat certain types of immunological and inflammatory diseases, including plaque psoriasis and psoriatic arthritis.[1,2] Plaque psoriasis is a chronically recurring, debilitating inflammatory disease that affects the skin, scalp, and nails.[1] It is characterized by erythrosquamous, itchy, and scaling lesions, and ranges in severity from mild to severe.[1] Psoriatic arthritis is a chronic inflammatory arthritis associated with psoriasis that can affect any joint in the body and commonly occurs with psoriasis.[2]

TIMs work by selectively blocking mechanisms involved in the inflammatory and immune response, although the specific mechanism can vary by TIM agent.[3,4] The US Food and Drug Administration (FDA) has approved or is currently evaluating drugs with 8 mechanisms of action in this class for treatment of plaque psoriasis, psoriatic arthritis, or both[5,6]:

- Tumor necrosis factor alpha (TNF-α) inhibitors: adalimumab (Humira), certolizumab pegol (Cimzia), etanercept (Enbrel), golimumab (Simponi), and infliximab (Remicade)
- Interleukin (IL)-17 inhibitors: bimekizumab (pipeline agent), brodalumab (Siliq), ixekizumab (Taltz), and secukinumab (Cosentyx)
- IL-23: inhibitors: guselkumab (Tremfya), risankizumab (Skyrizi), and tildrakizumab (Ilumya)
- Janus kinase inhibitors: tofacitinib (Xeljanz), and upadacitinib (Rinvoq)
- IL-12/23 inhibitors: ustekinumab (Stelara)
- Phosphodiesterase 4 (PDE4) inhibitor: apremilast (Otezla)
- Selective T-cell costimulatory modulators: abatacept (Orencia)
- Tyrosine kinase inhibitors: deucravacitinib (pipeline agent)

The FDA has approved biosimilar agents for adalimumab (Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz), etanercept (Erelzi, Eticovo), and infliximab (Avsola, Inflectra, Ixifi, Renflexis).

The Drug Effectiveness Review Project (DERP) is interested in an update of the previous 2020 report[7] of TIMs for plaque psoriasis and psoriatic arthritis indications, to inform policy and decision making about place in therapy with respect to these agents.

PICOS and Key Questions

This report focuses on adults with plaque psoriasis or psoriatic arthritis and identifies randomized controlled trials (RCTs) evaluating the comparative effectiveness and harms of FDA-approved TIM agents, as well as controlled cohort studies evaluating comparative harms. Outcomes of interest were measures of clinical improvement, disease remission, quality of life (QoL), adverse events (AEs), serious adverse events (SAEs), and other health outcome measures. This report also evaluates the effectiveness and harms (compared with placebo or another TIM agent) of selected pipeline agents.

This review addresses 4 Key Questions (KQs) focused on the effectiveness and harms of TIMs for plaque psoriasis and psoriatic arthritis (KQs 1 and 2), whether outcomes differ by personal characteristics (KQ3), and ongoing studies (KQ4).

Methods

We describe our complete methods in Appendix A. Briefly, we searched MEDLINE via PubMed, Cochrane Library, ClinicalTrials.gov, and several other websites, to identify eligible studies published or ongoing from May 1, 2019, through August 25, 2021, with active surveillance of the literature through December 31, 2021. We rated the risk of bias (RoB) of eligible studies using standard instruments adapted from national and international quality standards.[8-12] We used OpenEpi (version 3.01) to calculate risk ratios (RRs) and associated 95% confidence intervals (CIs) based on data provided in the study when not reported by authors. We rated the certainty of evidence (CoE) for each drug comparison and indication (plaque psoriasis or psoriatic arthritis) for 5 selected outcomes (i.e., disease remission, clinical improvement, QoL, AEs, and SAEs) using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.[13,14]

Key Findings

We included a total of 51 unique studies in 70 publications in this update:

- 18 new studies (in 22 publications)[15-36]
- 33 studies (in 38 publications) carried forward from the previous report[37-74]
- 10 new publications with additional data for 7 studies that were included in the previous report[75-84]

Forty-two studies (in 57 publications) evaluated TIMs for plaque psoriasis,[15,17,19,21-25,27-32,36-42,44-49,51-54,57-59,62-65,67-85] and 9 studies (in 13 publications) evaluated TIMs for psoriatic arthritis.[16,18,20,26,33-35,43,50,56,60,61,66]

Of the included studies, 40 were RCTs[15-26,37-41,43-47,49-54,60,62,64-69,71,73,74,86] and 11 were cohort studies.[27-32,55-59] We rated 3 RCTs[43,50,64] and 2 cohort studies[29,56] as high RoB; we rated the rest of the included studies as moderate RoB, primarily because of extensive manufacturer involvement in study design, execution, and reporting. Outcomes selected for GRADE ratings ranged from low to high CoE for most efficacy outcomes and very low to moderate for most harm outcomes. When we downgraded outcomes, it was generally because of serious or very serious imprecision (i.e., wide CI because of small sample size, rare events, or both).

In the section that follows, text highlighted in **purple font** represents no significant differences between drugs, text highlighted in **blue font** represents a significant difference favoring the intervention drug, and **orange font** represents a significant difference favoring the comparator drug.

Plaque Psoriasis

Comparative Effectiveness (KQ1)

We identified 25 RCTs[15,17,19,23,37,39,40,44-47,49,51,52,62,64,65,67-69,71,74] providing direct evidence of 18 different head-to-head TIM agent comparisons. Nearly all studies enrolled participants with at least 6 months history of moderate-to-severe plaque psoriasis. Nearly all studies reported disease remission or clinical improvement outcomes as primary study endpoints; the most reported outcomes were the Psoriasis Area and Severity Index (PASI) 90 and PASI 75 (reduction in PASI score of 90% and 75%, respectively).[87] A score of 0 (no impact) or 1 (very minimal impact) on the Physician's or Investigator's Global Assessment (PGA or IGA, respectively)

measure was also commonly used as either a primary or secondary outcome for disease remission.[87] Both measures are among the most-used validated measures of clinical improvement and disease remission in clinical trials evaluating psoriasis therapies.[87] More than half of the studies also reported QoL measures; most used the Dermatology Life Quality Index (DLQI). The DLQI is the most frequently used measure for evaluating QoL among persons afflicted with a variety of skin conditions; scores on the DLQI range from 0 to 30; a score of 0 or 1 indicates no effect of the skin condition on QoL.[87] Changes in QoL measures typically mirrored disease remission and clinical improvement findings in nearly all studies. Appendix D describes outcome measures used in included studies.

- *Apremilast vs. etanercept* (1 RCT[49]): **No significant difference** in clinical improvement (PASI 75) or QoL (DLQI) at 16 weeks; low CoE for both outcomes.
- *Brodalumab vs. ustekinumab* (2 RCTs[37,81,82]): **Brodalumab was more effective** for achieving disease remission and improving QoL at both 12 and 52 weeks (PASI 100: absolute risk differences (ARDs), 18 and 22 percentage points; DLQI: ARDs, 14 and 15 percentage points; high CoE).
- *Certolizumab pegol vs. etanercept* (1 RCT[15]): **Higher dose of certolizumab pegol (400 mg) was more effective** than etanercept at 12 weeks (PASI 75: calculated RR, 1.2; 95% CI, 1.04 to 1.5); **no differences between a lower dose (200 mg)** and etanercept (moderate CoE).
- *Etanercept vs. infliximab* (1 high-RoB RCT[64]): **Etanercept was less effective** for achieving clinical improvement at 24 weeks (PASI 75: 35% vs. 72%; very low CoE), **no difference in QoL** measures (very low CoE).
- *Etanercept vs. ixekizumab* (2 RCTs[68]): **Etanercept was less effective** for achieving clinical improvement at 12 weeks (PASI 75: ARDs, 31 and 48 percentage points) and for improving QoL (DLQI 0 or 1: ARDs, 20 and 30 percentage points); CoE was high for both outcomes.
- *Etanercept vs. secukinumab* (1 RCT[45]): **Etanercept was less effective** for achieving clinical improvement at 12 weeks (PASI 75: [etanercept] 44% vs. [300 mg secukinumab] 77% vs. [150 mg secukinumab] 67%; high CoE). Etanercept was also less effective at improving QoL (mean change DLQI: [etanercept] −7.9 vs. [300 mg secukinumab] −10.4 vs. [150 mg secukinumab] −9.7; moderate CoE). Etanercept was also less effective at maintaining disease remission at 52 weeks (PASI 75: [etanercept] 73% vs. [300 mg secukinumab] 84% vs. [150 mg secukinumab] 82%; high CoE).
- *Etanercept vs. tofacitinib (not FDA approved for psoriasis)* (1 RCT[62,63]): **Etanercept was more effective than 5 mg tofacitinib** at achieving clinical remission at 12 weeks (PASI 75: 59% vs. 40%, moderate CoE) and for QoL (DLQI 0 or 1: 75% vs. 66%; moderate CoE) but its **effectiveness compared with tofacitinib 10 mg was similar** (PASI 75: 59% vs. 64%; moderate CoE; DLQI 0 or 1: 75% vs. 78%; low CoE).
- *Etanercept vs. ustekinumab* (1 RCT[51]): **Etanercept was less effective** for clinical improvement at 12 weeks (PASI 75: [etanercept] 57% vs. [90 mg ustekinumab] 74%; vs. [45 mg ustekinumab] 68%; low CoE).
- *Guselkumab vs. adalimumab* (3 RCTs[69,73,74]): **Guselkumab was more effective** than adalimumab for disease remission at 16 weeks (PGA 0 or 1: ARD range, 16 to 28 percentage points; high CoE). Guselkumab was also more effective at improving QoL (DLQI 0 or 1: ARD range, 13 to 15 percentage points; moderate CoE).

- *Guselkumab vs. secukinumab* (1 RCT[44]): **Guselkumab was more effective** than secukinumab for disease remission at 48 weeks (PASI 90: 84% vs. 70%; moderate CoE); guselkumab was noninferior for clinical improvement at a combined endpoint that included 12 and 48 weeks (PASI 75: 85% vs. 80%; $P < .001$ for noninferiority; $P = .06$ for superiority); a higher PASI 90 response was observed for secukinumab at 12 weeks (69% vs. 76%) but no significance testing was done.
- *Ixekizumab vs. guselkumab* (1 RCT[17,36]): **Ixekizumab was more effective** for disease remission at 12 weeks (PASI 100: calculated RR, 1.7; 95% CI, 1.4 to 2.0), **but no differences evident at 24 weeks** (calculated RR, 0.96; 95% CI, 0.85 to 1.1; high CoE). Similar findings found for QoL as measured by DLQI 0 or 1 (high CoE).
- *Ixekizumab vs. secukinumab* (1 RCT[23]): **No difference** in disease remission at 24 weeks (PGA 0 or 1; calculated RR, 1.01; 95% CI, 0.81 to 1.3; moderate CoE).
- *Ixekizumab vs. ustekinumab* (1 RCT[47,48,79,83]): **Ixekizumab was more effective** than ustekinumab for disease remission at 12 weeks (PASI 90: 73% vs. 42%; moderate CoE) and at 52 weeks (PASI 90: 77% vs. 59%; moderate CoE). Ixekizumab was also more effective for improving QoL at 12 weeks (DLQI 0 or 1: 61% vs. 45%) and 52 weeks (71% vs. 57%); moderate CoE for both outcomes at both time points.
- *Risankizumab vs. adalimumab* (1 RCT[46]): **Risankizumab was more effective** than adalimumab for disease remission at 16 weeks (PASI 90: 72% vs. 47%; moderate CoE). Risankizumab was also more effective at improving QoL at 16 weeks (DLQI 0 or 1: 66% vs. 49%; moderate CoE).
- *Risankizumab vs. secukinumab* (1 RCT[19]): **No difference** in disease remission at 16 weeks, but risankizumab was more effective than secukinumab at 52 weeks (ARD, 30 percentage points; 95% CI, 21 to 39; moderate CoE).
- *Risankizumab vs. ustekinumab* (3 RCTs[52,67]): **Risankizumab was more effective** than ustekinumab for disease remission at 12 to 16 weeks (PASI 90: ARD range, 28 to 37 percentage points; moderate CoE). Risankizumab was also more effective at improving QoL at 12 to 16 weeks (DLQI 0 or 1: ARD range, 19 to 23 percentage points; moderate CoE).
- *Secukinumab vs. ustekinumab* (2 RCTs[39-42,77]): **Secukinumab was more effective** than ustekinumab for disease remission at 16 weeks (PASI 90: ARDs, 21 and 22 percentage points) and at 52 weeks (ARDs, 14 and 13 percentage points; high CoE). Secukinumab was also more effective at improving QoL at 16 weeks and 52 weeks (DLQI 0 or 1; high CoE).
- *Tildrakizumab vs. etanercept* (1 RCT[65]): **Tildrakizumab was more effective** for clinical improvement at 12 weeks (PASI 75: 200 mg tildrakizumab, 66%; 100 mg tildrakizumab, 61%; vs. etanercept, 48%) and at 28 weeks (PASI 75: both 200- and 100-mg dosages, 73% vs. etanercept, 54%; high CoE for both time points and doses). Tildrakizumab was also more effective than etanercept for improving QoL at both 12 weeks (moderate CoE) and 28 weeks (high CoE).

Comparative Harms (KQ2)

All RCTs included for KQ1 also reported on harms of TIM agents; in addition, we identified 10 cohort studies.[27-32,55,57-59] Overall, we observed **few differences in harms in head-to-head RCT comparisons of TIM agents**. In the RCT body of evidence, between-agent differences were typically just 1 of several harm outcomes reported when differences were present. **The rest of**

this section describes findings where at least 1 statistically significant difference was observed in AEs, SAEs, or other specific serious harms.

- *Apremilast vs. adalimumab* (1 cohort[59]): **Lower incidence of serious infection requiring hospitalization for apremilast** compared with adalimumab (hazard ratio [HR], 0.31; 95% CI, 0.15 to 0.65; very low CoE).
- *Apremilast vs. etanercept* (1 RCT,[49] 1 cohort[28]*)*: **Higher incidence of AEs for apremilast** (calculated RR, 1.3; 95% CI, 1.05 to 1.7; low CoE). **No difference for SAEs** (RR, 1.5; 95% CI, 0.26 to 8.7; very low CoE). **No difference in serious infections** in the new cohort study (adjusted HR, 0.83; 95% CI, 0.63 to 1.10, very low CoE).
- *Apremilast vs. infliximab* (1 cohort[28]): **Lower incidence of serious infection with apremilast** (adjusted HR, 0.46; 95% CI, 0.34 to 0.63, very low CoE).
- *Certolizumab pegol vs. infliximab* (1 cohort[28]): **Lower incidence of serious infection with certolizumab pegol** (adjusted HR, 0.64; 95% CI, 0.46 to 0.91, very low CoE).
- *Certolizumab pegol vs. ustekinumab* (2 cohorts[27,28]): **Higher incidence of serious infection for certolizumab pegol**, but it was only statistically significant in 1 of 2 studies (adjusted HR, 1.45; 95% CI, 1.03 to 2.04 in 1 study; HR, 1.09; 95% CI, 0.68 to 1.75 in other study; very low CoE).
- *Etanercept vs. adalimumab* (2 cohorts[28,59,88]*)*: **Lower incidence of serious infection for etanercept** (HR, 0.76; 95% CI, 0.61 to 0.94 in 1 study; adjusted HR, 0.82, 95% CI, 0.72 to 0.93 in other study; very low CoE)[59]; **no difference in major cardiovascular events** (1 study; adjusted incidence rate ratio [IRR], 0.62; 95% CI, 0.18 to 1.72; very low CoE).[88]
- *Etanercept vs. infliximab* (1 RCT,[64] 1 cohort[28]): **Lower risk of serious infection with etanercept in the cohort study** (adjusted HR, 0.56; 95% CI, 0.46 to 0.67; very low CoE); however, **no difference in SAEs** in the RCT but results were imprecise (RR, 0.36; 95% CI, 0.08 to 1.60; very low CoE), and no difference in overall AEs (very low CoE).
- *Etanercept vs. ustekinumab* (1 RCT,[51] 2 cohorts[27,28]): **No significant differences in overall AEs or SAEs** in the RCT (low CoE); **higher incidence of serious infection with etanercept** in the cohort studies (very low CoE).
- *Infliximab vs. adalimumab* (2 cohorts[28,59]): **Higher incidence of serious infection for infliximab** (HR, 1.9; 95% CI, 1.01 to 3.60 in 1 study; adjusted HR, 1.47; 95% CI, 1.24 to 1.74 in other study; very low CoE).
- *Infliximab vs. ustekinumab* (2 cohorts[27,28]): **Increased incidence of serious infection with infliximab** (adjusted HR, 2.9; 95% CI, 1.8 to 4.7 in 1 study; adjusted HR, 2.3; 95% CI, 1.9 to 2.8 in other study; very low CoE).
- *Ixekizumab vs. infliximab* (1 cohort[28]): **Lower incidence of serious infection with ixekizumab** (adjusted HR, 0.46; 95% CI, 0.27 to 0.77; very low CoE).
- *Risankizumab vs. ustekinumab* (3 RCTs[52,67]): One RCT reported **no significant differences in AEs or SAEs**.[52] Two RCTs reported some differences, but not across all time periods evaluated. For overall AEs, **fewer AEs observed for risankizumab in the later time period (weeks 17 to 52) of 1 study** (RR, 0.75; 95% CI, 0.11 to 0.77; low CoE), and **fewer SAEs observed for risankizumab in the early time period (weeks 0 to 16) of the other study** (RR, 0.29; 95% CI, 011 to 0.77; low CoE).
- *Secukinumab vs. adalimumab* (1 cohort[28]): **Lower incidence of serious infection with secukinumab** (adjusted HR, 0.77; 95% CI, 0.62 to 0.96; very low CoE).

- *Secukinumab vs. infliximab* (1 cohort[28]): **Lower incidence of serious infection with secukinumab** (adjusted HR, 0.53; 95% CI, 0.41 to 0.68; very low CoE).
- *Tildrakizumab vs. etanercept* (1 RCT[65]): **Fewer overall AEs for tildrakizumab** compared with etanercept during weeks 13 to 28 (RR, 0.80; 95% CI, 0.68 to 0.93), fewer AEs for 100-mg, but not 200-mg dose during weeks 0 to 12 (moderate CoE). **No difference in incidence of SAEs** during either time period (low CoE).
- *Ustekinumab vs. adalimumab* (2 cohorts[28,59]): **Fewer serious infections with ustekinumab** (HR, 0.70; 95% CI, 0.49 to 1.00 in 1 study; adjusted HR, 0.65; 95% CI, 0.56 to 0.76 in other study; very low CoE).

Effectiveness and Harms From Pipeline TIM Agents

Effectiveness and harms from 7 RCTs[21,22,24,25,38,53,54] of 2 pipeline TIM agents (bimekizumab and deucravacitinib) were available; CoE ratings for efficacy and harms ranged from very low to moderate.

Psoriatic Arthritis

Comparative Effectiveness (KQ1)

We identified 7 RCTs[16,18,26,33,34#,35,43,50,60,61,66] providing direct evidence of 6 different head-to-head TIM agent comparisons. Of these, 3 RCTs are new to this update.[16,18,26,33-35] All studies enrolled participants with active psoriatic arthritis; 1 study[43] specifically required active enthesitis (i.e., a common symptom in psoriatic arthritis involving inflammation of the sites where tendon or ligaments attach to bones). We rated 2 RCTs[43,50] as high RoB for various critical methodological flaws; we rated the rest as moderate RoB because of extensive manufacturer involvement in study design, execution, and reporting. Nearly all studies reported measures of clinical improvement as primary study endpoints; the most reported outcomes were the American College of Rheumatology 20 criteria (ACR20) response (at least 20% improvement in swollen and tender joint count, and at least 20% improvement in 3 of the following 5 outcomes: inflammatory biomarker, IGA, patient global assessment [PtGA], pain, disability). QoL outcomes were reported in 4 of the RCTs.[26,35,43,60] Appendix D describes outcome measures used in included studies.

- *Adalimumab vs. etanercept or infliximab* (1 RCT[50]): **No differences** in ACR20 response at 1 year (no statistical significance testing; very low CoE).
- *Adalimumab vs. tofacitinib* (1 RCT[60]): **Numerically lower clinical improvement at 12 months with adalimumab** compared with participants treated with tofacitinib 10 mg but **no differences compared with participants treated with tofacitinib 5 mg** (ACR20: 60% vs. 70% vs. 68%; low CoE). **Numerically lower skin disease remission at 12 months with adalimumab** compared with tofacitinib 10 mg, but **no differences compared with tofacitinib 5 mg** (PASI 75: 56% vs. 67% vs. 56%; low CoE). **Numerically higher improvement in QoL** (36-item Short Form Health Survey [SF-36] Physical Health Component Score [PCS]) for **adalimumab** compared with tofacitinib 10 mg or tofacitinib 5 mg (6.2 vs. 5.7 vs. 5.5; low CoE).
- *Ixekizumab vs. adalimumab* (2 RCTs[18,33,34,66]): **Numerically lower clinical improvement in arthritis at 24 weeks for adalimumab** compared with ixekizumab every 2 or 4 weeks (ACR20: [adalimumab] 57% vs. [ixekizumab every 2 weeks] 62% vs. [ixekizumab every 4 weeks] 58%; no statistical testing); the other study had a calculated RR of 0.96 (95% CI, 0.86 to 1)

(moderate CoE). A **numerically lower skin disease remission response with adalimumab** compared with ixekizumab every 2 weeks or every 4 weeks (PASI 75: 54% vs. 80% vs. 71%; no statistical testing); the other study had a calculated RR of 1.2 (95% CI, 1.06 to 1.30) (moderate CoE).

- *Secukinumab vs. adalimumab* (1 RCT[16,35]): **No difference in arthritis clinical improvement** at 52 weeks (ACR20: calculated RR, 1.1; 95% CI, 0.98 to 1.20; moderate CoE); **larger clinical improvement in skin disease with secukinumab** (PASI 90: calculated RR, 1.5; 95% CI, 1.3 to 1.7; moderate CoE).
- *Upadacitinib vs.* adalimumab (1 RCT[26]): At 12 weeks, a **larger proportion showed improvement in arthritis** (ACR 20: calculated RR, 1.2; 95% CI, 1.1 to 1.3) **with upadacitinib 30-mg dosage** but no difference with a 15-mg dosage (moderate CoE); larger improvement in QoL (Health Assessment Questionnaire–Disability Index) with a upadacitinib 30-mg but not a 15-mg dosage (moderate CoE).
- *Ustekinumab vs. TNF-α inhibitors* (1 RCT[43]): At 24 weeks, **higher proportion achieved enthesitis remission** (Spondyloarthritis Research Consortium of Canada Enthesitis Index: 74% vs. 42%; very low CoE) and skin disease remission (PASI 90: 86% vs. 29%; very low CoE), **but not arthritis remission** (tender joint count, 54% vs. 46%; *P* = .78; swollen joint count, 59% vs. 46%; *P* = .38; very low CoE). Larger improvement in QoL as measured by SF-36 PCS for ustekinumab (magnitude not reported), but no statistically significant difference in improvement in QoL as measured by the SF-36 Mental Health Component Score [MCS]; very low CoE).

Comparative Harms (KQ2)

Six of 7 RCTs included for KQ1 also reported harms.[16,18,26,33,34#,35,50,56,60,61,66] We observed **few differences in harms in head-to-head trials of TIM agents** (very low to moderate CoE for overall AEs and SAEs). Some differences were observed between agents in injection-site reactions or withdrawals due to AEs, but these were noted in single studies of single comparisons. **In the rest of this section, we highlight comparisons with a significant difference in overall AEs or SAEs.**

- *Adalimumab vs. etanercept vs. infliximab* (1 RCT,[50] 1 cohort[56]): **Fewer AEs with adalimumab vs. etanercept** (RR, 0.38; 95% CI, 0.17 to 0.84), **fewer AEs with adalimumab vs. infliximab** (RR, 0.23; 95% CI, 0.11 to 0.49), and **more AEs with infliximab vs. etanercept** (RR, 1.6; 95% CI, 1.1 to 2.4; very low CoE for all comparisons). One cohort study[56] reported a **higher incidence of tuberculosis for infliximab vs. adalimumab or etanercept** (very low CoE).
- *Upadacitinib vs. adalimumab* (1 RCT[26]): **More AEs with upadacitinib** (calculated RR, 1.1; 95% CI, 1.02 to 1.20; moderate CoE); **no difference in SAEs** (calculated RR, 1.6; 95% CI, 0.9 to 3.0; low CoE).
- Efficacy and harms of pipeline agents were limited to 1 placebo-controlled trial of bimekizumab[20]; CoE ratings ranged from very low to low.

Efficacy and Safety Among Subgroups (KQ3)

Relevant subgroup analyses were available for 3 comparisons for plaque psoriasis[75,76,80] and for 1 comparison for psoriatic arthritis.[18]

- *Brodalumab vs. ustekinumab for plaque psoriasis*: No differences in comparative efficacy or safety in post hoc subgroup analysis of participants with BMI < 30 kg/m^2 versus those with BMI ≥ 30 kg/m^2.[76]
- *Guselkumab vs. secukinumab for plaque psoriasis*: Guselkumab was superior to secukinumab overall and in all subgroups evaluated based on age, weight, BMI, severity of disease, body area affected, and prior medication use.[80]
- *Tildrakizumab vs. etanercept for plaque psoriasis*: No differences in comparative efficacy for participants with metabolic syndrome compared with those without metabolic syndrome.[75]
- *Ixekizumab vs. adalimumab for psoriatic arthritis*: Ixekizumab was more effective than adalimumab for individuals with and without concomitant use of methotrexate, although the difference was not statistically significant in concomitant users.[18]

Ongoing Studies (KQ4)

We identified 17 ongoing studies.[89-105] This includes 12 RCTs (6 for plaque psoriasis[89-94] and 6 for psoriatic arthritis[95-100]) and 5 observational studies (3 for plaque psoriasis,[101,103,104] 1 for psoriatic arthritis,[102] and 1 that included participants with either condition[105]).

Conclusions

For plaque psoriasis, the largest body of comparative evidence continues to be for etanercept and ustekinumab compared with other TIM agents, although new studies are available in this update for ixekizumab, secukinumab, and risankizumab. For clinical improvement and disease remission outcomes, moderate- and high-certainty evidence suggests etanercept is less effective than certolizumab pegol, ixekizumab, secukinumab, and tildrakizumab. Moderate- and high-certainty evidence also suggests ustekinumab is less effective than brodalumab, ixekizumab, risankizumab, and secukinumab. Other comparisons with moderate or high CoE for clinical improvement and disease remission favor guselkumab: a) versus adalimumab; b) versus secukinumab (at later time points); and c) versus ixekizumab (at early but not later time points). Moderate-certainty evidence suggests no difference between ixekizumab and secukinumab. Moderate-certainty evidence favors risankizumab versus adalimumab and versus secukinumab (at later time points). Few differences in harms among TIM agents were observed, based on very low to moderate CoE.

For psoriatic arthritis, limited head-to-head comparisons are available. The only moderate-certainty head-to-head evidence compared ixekizumab, secukinumab, or upadacitinib with adalimumab; all were superior to adalimumab for improving skin disease, but only higher doses of upadacitinib were superior for improving arthritis symptoms. However, upadacitinib had more AEs compared with adalimumab. Few other differences in harms among TIM agents were observed, based on very low to moderate CoE.

Identified ongoing studies for plaque psoriasis and psoriatic arthritis will address some gaps in the evidence by evaluating new comparisons or potentially increasing our CoE for existing comparisons. The completion dates for these studies range from November 2020 to July 2024.

List of Brand Names and Generics

Table 1. Included Drugs and Biosimilars for Treatment of Plaque Psoriasis and Psoriatic Arthritis

Generic Name	Trade Name	Mechanism	Route	Approved Population[a]
Abatacept	Orencia	Selective T-cell costimulation modulator	IV or SC	Psoriatic arthritis
Adalimumab	Humira	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab-adaz	Hyrimoz	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab-adbm	Cyltezo	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab—afzb	Abrilada	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab-atto	Amjevita	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab-bwwd	Hadlima	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Adalimumab-fkjp	Hulio	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Apremilast	Otezla	PDE4 inhibitor	PO	Plaque psoriasis Psoriatic arthritis
Brodalumab	Siliq	IL-17RA inhibitor	SC	Plaque psoriasis
Certolizumab pegol	Cimzia	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Etanercept	Enbrel	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Etanercept-szzs	Erelzi	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Etanercept-ykro	Eticovo	TNF-α inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Golimumab	Simponi/ Simponi ARIA	TNF-α inhibitor	SC	Psoriatic arthritis
Guselkumab	Tremfya	IL-23 inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Infliximab	Remicade	TNF-α inhibitor	IV	Plaque psoriasis Psoriatic arthritis
Infliximab-abda	Renflexis	TNF-α inhibitor	IV	Plaque psoriasis Psoriatic arthritis
Infliximab-axxq	Avsola	TNF-α inhibitor	IV	Plaque psoriasis Psoriatic arthritis

Generic Name	Trade Name	Mechanism	Route	Approved Population[a]
Infliximab-dyyb	Inflectra	TNF-α inhibitor	IV	Plaque psoriasis Psoriatic arthritis
Infliximab-qbtx	Ixifi	TNF-α inhibitor	IV	Plaque psoriasis Psoriatic arthritis
Ixekizumab	Taltz	IL-17A inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Risankizumab	Skyrizi	IL-23 inhibitor	SC	Plaque psoriasis
Secukinumab	Cosentyx	IL-17A inhibitor	SC	Plaque psoriasis Psoriatic arthritis
Tildrakizumab	Ilumya	IL-23 inhibitor	SC	Plaque psoriasis
Tofacitinib	Xeljanz Xeljanz XR	JAK inhibitor	PO	Psoriatic arthritis
Upadacitinib	Rinvoq	JAK inhibitor	PO	Psoriatic arthritis
Ustekinumab	Stelara	IL-12/23 p40 inhibitor	Initial dose IV then SC	Plaque psoriasis Psoriatic arthritis
Pipeline drugs				
Bimekizumab	None	IL-17A and IL-17F inhibitor	IV	Not yet approved (PDUFA date delayed from 10/15/2021)
Deucravacitinib	None	TYK2 inhibitor	PO	Not yet approved (PDUFA date 09/10/2022)

Notes. [a] Details of approved indications for each drug can be found in the full prescribing information. Some drugs may be approved for indications other than psoriasis or psoriatic arthritis.
Abbreviations. IL: interleukin; IV: intravenous; JAK: Janus kinase; PDE4: phosphodiesterase 4; PDUFA: Prescription Drug User Fee Act; PO: oral; RA: receptor A; SC: subcutaneous; TNF-α: tumor necrosis factor alpha; TYK2: tyrosine kinase 2; XR: extended release.

Background

Targeted immune modulators (TIMs) are a category of medications used in the treatment of certain types of immunological and inflammatory diseases, including rheumatoid arthritis, ankylosing spondylitis, Crohn disease, ulcerative colitis, plaque psoriasis, and psoriatic arthritis.[1,2] TIMs work by selectively blocking mechanisms involved in the inflammatory and immune response.[3] The US Food and Drug Administration (FDA) approved the first TIM for psoriatic arthritis (etanercept) in 2002 and the first TIM for psoriasis (alefacept) in 2003.[5,106] Since then, the FDA has approved numerous agents for these conditions, including biosimilars.[5] Table 1 summarizes currently available TIMs approved in the US for plaque psoriasis and psoriatic arthritis.[1,2,4-6]

Adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab bind to both the circulating and transmembrane forms of tumor necrosis factor alpha (TNF-α), inhibiting its biological activity.[1,2,4,5,107,108] Biosimilars are available for adalimumab, etanercept, and infliximab. Adalimumab, certolizumab, etanercept, and infliximab are all FDA-approved for both plaque psoriasis and psoriatic arthritis. Golimumab is only FDA-approved for psoriatic arthritis.

Secukinumab and ixekizumab are human immunoglobulin G1 (IgG1) and IgG4 monoclonal antibodies, respectively, that selectively bind to the interleukin (IL)-17A cytokine and inhibit their interaction with the IL-17 receptor, thus inhibiting the release of proinflammatory cytokines and chemokines.[1,2,4,5,107,108] Brodalumab is another human IgG monoclonal antibody to the IL-17A receptor, which inhibits the activity of IL-17A, plus IL-17F, IL-17A/F, and IL-17E.[1,108] Ixekizumab and secukinumab are FDA-approved for plaque psoriasis and psoriatic arthritis, while brodalumab is approved only for plaque psoriasis. Because of a potential risk for suicidal ideation, the FDA requires a Risk Evaluation and Mitigation Strategy program for patients and prescribers of brodalumab.[109] Finally, bimekizumab is a dual IL-17A and IL-17F inhibitor that is not yet approved by the FDA. The target date for FDA approval of this pipeline agent was October 15, 2021, but it was delayed by the FDA due to COVID-19–related delays in European manufacturing site inspections.[110]

Tildrakizumab, risankizumab, and guselkumab are humanized IgG1 monoclonal antibodies that act as IL-23 antagonists by selectively binding to the P19 subunit of IL-23.[1,2,4,5] Tildrakizumab and risankizumab are approved for plaque psoriasis, and guselkumab is also approved for psoriatic arthritis. Trials of 1 pipeline agent with a similar mechanism of action (mirikizumab) that we included in the last update were discontinued by the manufacturer; it will no longer be pursuing FDA approval for this drug.[111]

Ustekinumab is a human monoclonal antibody that binds to the p40 protein subunit used by both the IL-12 and IL-23 cytokines.[1,2,4,5,107,108] This drug has current FDA approval for plaque psoriasis and psoriatic arthritis.

Tofacitinib and upadacitinib are small molecules directed against the Janus kinase (JAK) signal transducer and activator of transcription proteins pathway.[1,2,4,5,107,108,112] Unlike other biologics that may selectively block a single cytokine or integrin, JAK inhibitors block multiple cytokines, resulting in a wider effect on inflammation.[112,113] Tofacitinib is approved for the treatment of psoriatic arthritis; in 2015, the FDA declined to approve tofacitinib for a plaque psoriasis pending

additional efficacy and long-term safety data.[113] As of this update, we identified no evidence that the manufacturer plans to resubmit for this indication. Upadacitinib was approved for psoriatic arthritis in December 2021. Trials of 1 pipeline JAK inhibitor (filgotinib) for psoriatic arthritis that was included in the last update were discontinued by the manufacturer; it will no longer be pursuing FDA approval for this indication.[114]

Apremilast is an orally available phosphodiesterase 4 (PDE4) inhibitor that modulates production of a wide range of inflammatory mediators and is FDA-approved for psoriasis and psoriatic arthritis.[1,5,107,108]

The immunosuppressant agent abatacept exerts immune regulation by interfering with T lymphocyte activation.[2,5,107,108] Abatacept is FDA-approved for psoriatic arthritis.

One pipeline tyrosine kinase 2 inhibitor drug, deucravacitinib, is in active development by the manufacturer, and the target date for FDA approval date is September 2022.[115] Finally, a pipeline agent that was included in the prior update (remtolumab, a dual TNF-α/IL-17 inhibitor) is no longer being developed by its manufacturer.[116]

Plaque Psoriasis

Plaque psoriasis is a chronically recurring, debilitating inflammatory disease that affects the skin, scalp, and nails.[1,117] It is characterized by erythrosquamous scaling and itchy lesions and ranges in severity from mild to severe.[1,117] Plaque psoriasis is the most common type; other types include guttate, erythrodermic, and pustular psoriasis.[1,118] Patients with moderate-to-severe disease experience significant deterioration of quality of life (QoL),[119] and up to 20% have depression, including some with suicidal ideation and behavior.[1] The exact pathogenesis of plaque psoriasis is still unknown; however, pathophysiological evidence suggests that an overproduction of proinflammatory cytokines, particularly IL-17 and IL-23, plays an important role.[1,120,121]

The severity of plaque psoriasis is most commonly classified based on the percentage of body surface area (BSA) involved.[119,122] Mild psoriasis is defined as affecting less than 5% of the BSA; moderate psoriasis affects 5% to 10%; and severe psoriasis is defined as affecting more than 10% of the BSA.[119,122] The goal of plaque psoriasis treatment is to gain control of the disease process, decrease the percentage of BSA involved, and achieve and maintain long-term remission.[107] Systemic therapies are generally recommended when 10% or more BSA is affected, topical therapy has failed, or special sites, such as scalp, palms, soles, or genitalia, are involved.[1]

Psoriatic Arthritis

Psoriatic arthritis is a chronic inflammatory arthritis often associated with the skin disease psoriasis, but the presentation is variable.[2] Symptoms include pain and stiffness in the affected joint as well as joint-line tenderness, swelling, and sometimes loss of range of motion.[2] In some individuals with psoriatic arthritis, dactylitis, enthesitis, spondylitis, sacroiliitis, and uveitis may also occur.[2] The Classification Criteria for Psoriatic Arthritis defines psoriatic arthritis but was mainly developed for research purposes.[2]

The etiology and pathogenesis of psoriasis and psoriatic arthritis are not completely understood, but genetic, immunological, and environmental factors are all likely to play a role.[2,123] The first line of treatment for both conditions is nonsteroidal anti-inflammatory drugs (NSAIDs), often

combined with intraarticular injections for mild cases.[2] In persons with moderate-to-severe symptoms, disease-modifying antirheumatic drugs (DMARDs) may be necessary, including conventional (methotrexate, leflunomide, and sulfasalazine) or biologic agents.[2,108]

The Drug Effectiveness Review Project (DERP) is interested in an update of the previous 2020 report[7] for these indications to inform policy and decision making about place in therapy with respect to these agents.

PICOS

Population

- Adults with plaque psoriasis
- Adults with psoriatic arthritis

Interventions

- TIMs and respective biosimilars that have FDA approval for the treatment of plaque psoriasis or psoriatic arthritis, and select pipeline drugs likely to be approved soon (Table 1)

Comparators

- FDA-approved drugs: another listed TIM intervention (head-to-head comparison)
- For pipeline drugs: any listed TIM, standard of care, placebo

Outcomes

- Health outcomes
  - QoL
  - Functional capacity
  - Productivity, ability to sustain employment
  - Clinical improvement
  - Disease remission
  - Pain
  - Reduction in number of swollen or tender joints
  - Reduction in disease-related hospitalizations
  - Reduction in disease-specific mortality
  - Rebound/flare
  - Joint destruction
  - Steroid withdrawal
- Harms
  - Overall adverse events (AEs)
  - Withdrawals due to AEs
  - Serious adverse events (SAEs)
  - Specific AEs (e.g., lymphoma, all malignancies, serious infectious diseases, herpes zoster, opportunistic infections, congestive heart failure)
  - Mortality

Study Designs

- Randomized controlled trials (RCTs) with ≥ 12-week study duration
- Retrospective and prospective cohort studies comparing an intervention type to another for outcomes on harms
  - > 12-week study duration
  - Minimum total sample size of 1,000
  - Report adjusted head-to-head comparisons (this criterion was new for this update)

Key Questions

KQ1. What is the comparative effectiveness of TIMs to treat plaque psoriasis and psoriatic arthritis?

KQ2. What are the comparative harms of TIMs to treat plaque psoriasis and psoriatic arthritis?

KQ3. Do the included drugs differ in their effectiveness or harms in the following subgroups: age and racial groups, gender, patients with comorbidities, patients taking other commonly prescribed drugs, or in patients with early versus established disease?

KQ4. What are the characteristics of ongoing studies of TIMs to treat plaque psoriasis and psoriatic arthritis?

Methods

We describe our complete methods in Appendix A. Briefly, we searched MEDLINE via PubMed, Cochrane Library, ClinicalTrials.gov, and several other websites to identify eligible published or ongoing studies from May 1, 2019, through August 25, 2021, with active surveillance of the literature through December 31, 2021. We rated the risk of bias (RoB) of eligible studies using standard instruments adapted from national and international quality standards.[8-12] We used OpenEpi (version 3.01) to calculate risk ratios (RRs) and associated 95% confidence intervals (CIs) based on data provided in the study when not reported by authors. We rated the certainty of evidence (CoE) for each drug comparison and indication (plaque psoriasis or psoriatic arthritis) for 5 selected outcomes (i.e., disease remission, clinical improvement, QoL, overall AEs, and SAEs) using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.[13,14]

Findings

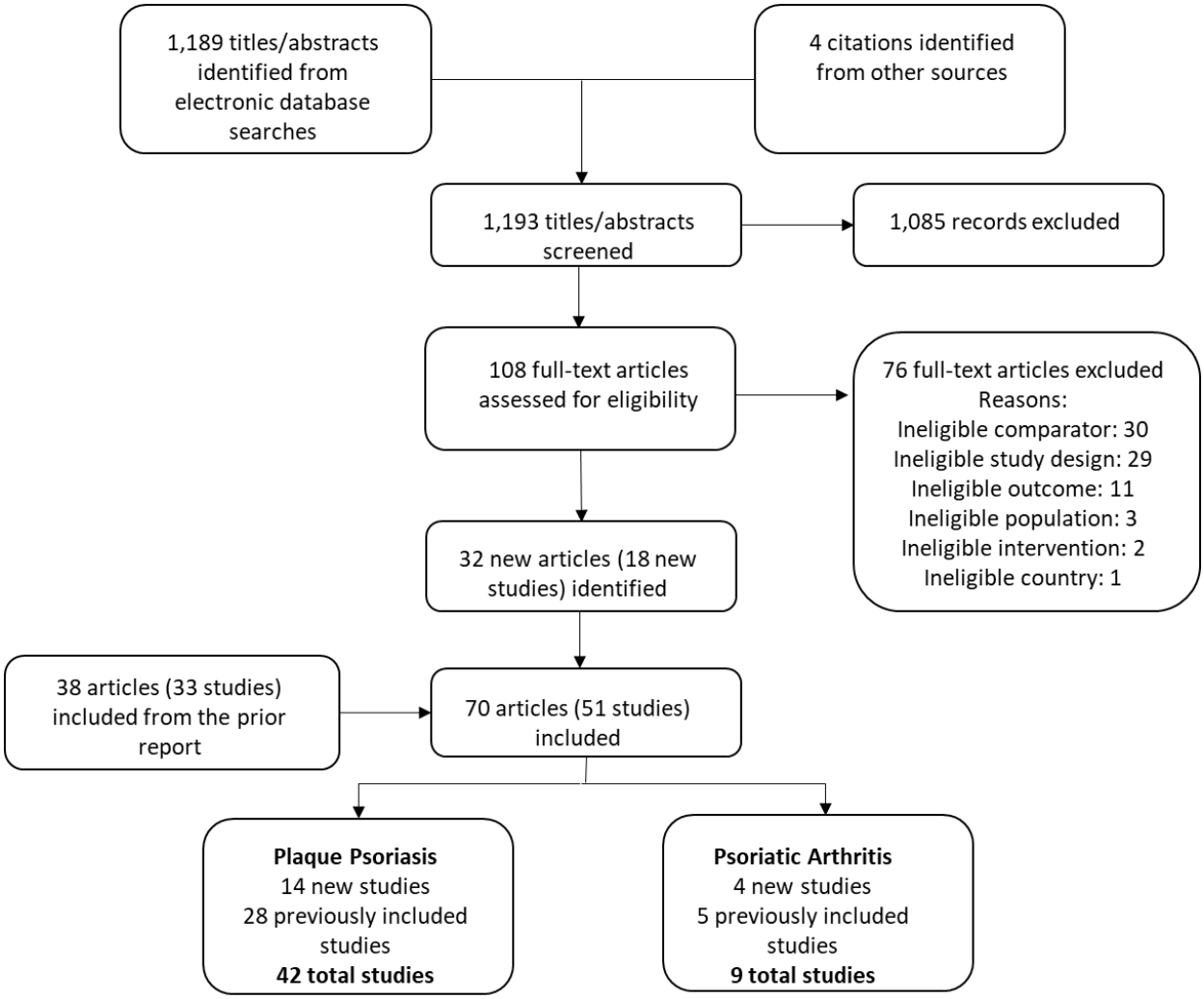
We included a total of 51 unique studies in 70 publications (Figure 1; Appendix E):

- 18 studies (in 22 publications) new to this update[15-36]
- 33 studies (in 38 publications) carried forward from the previous report[37-74]
- 10 new publications with additional data for 7 studies that were included in the previous report[75-84]

We excluded 5 studies that were included in the previous review.[86,88,124-126] Three of these studies reported on pipeline drugs that are no longer in development for psoriasis or psoriatic arthritis (mirikizumab,[86] remtolumab,[124] and filgotinib[125]). The other 2 were excluded for methodologic consistency with the current update; they were both cohort studies reporting on incidence of harms, but did not report adjusted estimates for head-to-head comparisons.[88,126]

Appendix F provides the bibliography of studies identified in the update search but which we excluded at the full-text review stage. We rated 3 RCTs[43,50,64] and 2 cohort studies[29,56] as high RoB; we rated the rest of the included RCTs and cohort studies as moderate RoB.[15-28,30-42,44-49,51-55,57-63,65-84]

Figure 1. Literature Flow Diagram



Forty-two studies (in 57 publications) evaluated TIMs for plaque psoriasis[15,17,19,21-25,27-32,36-42,44-49,51-54,57-59,62-65,67-85] and 9 studies (in 13 publications) evaluated TIMs for psoriatic arthritis.[16,18,20,26,33-35,43,50,56,60,61,66]

Across this body of evidence, the most common outcomes used to assess clinical improvement and disease remission for psoriasis were the Psoriasis Area and Severity Index (PASI) and the Physician's or Investigator's Global Assessment (PGA or IGA).[87] The PASI score is based on the extent of skin area involved, severity of erythema, desquamation, and plaque induration; the score can range from 0 (no disease) to 72 (maximum disease).[87] Clinical improvement and disease

remission is reported based on PASI response; a PASI 50 response refers to a 50% reduction in PASI score from baseline. Likewise, a PASI 90 response refers to a 90% reduction in score from baseline.[87] The PGA/IGA is scale where 0 represents "clear skin" and 5 or 6 represents "severe and extensive involvement."[87] The Dermatology Life Quality Index (DLQI) is the most frequently used validated measure for evaluating QoL among individuals living with a variety of skin conditions.[87] Scores on the DLQI range from 0 to 30; a score of 0 or 1 indicates the skin condition has no effect on QoL.[87] For descriptions of additional instruments and measures used across this body of evidence, see Appendix D.

The most common outcome used to assess clinical improvement and disease remission in psoriatic arthritis was the American College of Rheumatology (ACR) score. The ACR score is a composite measure of disease activity that considers the number of tender joints, the number of swollen joints, a patient's global assessment, a PGA, functional ability, pain, and inflammatory markers (e.g., erythrocyte sedimentation rate, C-reactive protein).[127] An ACR20 response is defined as a 20% improvement in the number of tender and swollen joints and a 20% improvement in at least 3 of the other score elements.[127] The Health Assessment Questionnaire (HAQ) was the most-used instrument to assess QoL in psoriatic arthritis trials[128]; additional instruments and measures used across this body of evidence are described in Appendix D.

Lastly, during surveillance we identified 1 late-breaking pipeline study comparing deucravacitinib to placebo (NCT03881059) published as this report was undergoing finalization; it is listed in the table of ongoing studies and will be captured in the next update of this topic.[98,129]

Plaque Psoriasis

We identified 32 RCTs[15,17,19,21-25,37-40,44-47,49,51-54,62,64,65,67-69,71,74] evaluating the effectiveness, comparative effectiveness, or harms of TIMs (including pipeline agents), and 10 cohort studies[27-32,57-59,85] evaluating the comparative harms of TIMs. Of these, 8 RCTs[15,17,19,21-25] are new to this update, and 5 cohort studies[27-30,32] are new to this update. Table 2 shows the Summary of Findings (GRADE) for comparative effectiveness and harms of TIMs from RCTs only. Appendix C, Table C1 provides detailed evidence profiles, including CoE ratings that incorporate cohort studies.

Table 2. Summary of Findings (GRADE) of TIMs for Plaque Psoriasis from RCTs

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)	No difference
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)	No difference
Certolizumab vs. with etanercept		
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors higher dose of certolizumab
AE (1 RCT)	●●●○ (moderate)	No difference
SAE (1 RCT)	●●○○ (low)	No difference
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)	No difference

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. tofacitinib		
Disease remission (1 RCT)	●●●○ (moderate)	Favors etanercept[b]
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors etanercept[b]
QoL (1 RCT)	●●○○ (low)	Favors etanercept[b]
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (low)	No difference

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		
Disease remission (1 RCT)	●●●○ (moderate)	Favors guselkumab at later time points[c]
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●●○○ (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

Outcome	Certainty of Evidence	Relationship[a]
Ixekizumab vs. secukinumab		
Disease remission (1 RCT)	●●●○ (moderate)	No difference
Clinical improvement (1 RCT)	●●●○ (moderate)	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. 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

Outcome	Certainty of Evidence	Relationship[a]
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
Tildrakizumab vs. etanercept		
Clinical improvement (1 RCT)	●●●● (high)	Favors tildrakizumab
QoL (1 RCT)	●●●● (high)	Favors tildrakizumab
AEs (1 RCT)	●●●○ (moderate)	Favors tildrakizumab
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] For lower dose of tofacitinib (5 mg), but no difference for higher dose (10 mg). [c] Some secondary endpoints favored secukinumab at early (12-week) time point.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event; TIM: targeted immune modulator.

Comparative Efficacy (KQ1)

Twenty-five RCTs[15,17,19,23,37,39,40,44-47,49,51,52,62,64,65,67-69,71,74] reported efficacy outcomes for 18 different head-to-head TIM agent comparisons. Nearly all studies enrolled participants with a history of at least 6 months of moderate-to-severe plaque psoriasis. We rated 1 RCT as high RoB due to insufficient blinding and switching of treatments.[64] We rated the rest as moderate RoB, primarily due to extensive manufacturer involvement in study design, execution, and reporting. In this section, we describe efficacy findings organized by drug comparisons. Table 3 provides a summary of this evidence base and summarizes the findings. Appendix B, Tables B1 and B2 provide detailed study characteristics and results, and Appendix D describes outcome measures used in included RCTs.

Apremilast vs. Etanercept

We did not identify any new RCTs for this update.

The previous review included 1 head-to-head moderate-RoB RCT (LIBERATE)[49] comparing apremilast 30 mg twice daily with etanercept 50 mg once weekly and with placebo, in 250 biologically naïve participants with moderate-to-severe chronic plaque psoriasis for 16 weeks. This dosage of etanercept (50 mg once per week) is the standard labeled dose in Europe[130]; however, it is less than the recommended dosage in the US (twice weekly for 3 months, followed by 50 mg once a week).[131]

The primary endpoint for the trial was the PASI 75 response rate.[49] At week 16, participants treated with apremilast had no difference in response compared with participants receiving etanercept (40% vs. 48%; $P = .26$).[49] For key secondary outcomes authors observed some differences, but statistical significance testing was not reported (PGA 0 or 1, 22% vs. 29%; PASI 50, 63% vs. 83%).[49] Similar results were seen for the PASI 90, an exploratory endpoint (15% vs. 21%; *P* value not reported [NR]).[49] For other secondary outcomes such as the percent BSA involvement or the DLQI score, participants on apremilast or etanercept had no difference in improvements.[49]

Brodalumab vs. Ustekinumab

We did not identify any new RCTs for this update; however, we did identify 3 new companion articles[76,81,82] to the 2 previously included RCTs for this comparison.[37]

AMAGINE-2 and AMAGINE-3 were large (> 1,000 participants), phase 3, multicenter moderate-RoB RCTs comparing brodalumab (210 mg at weeks 0, 1 and 2, then every 2 weeks) with ustekinumab (45 mg for participants with a body mass ≤ 100 kg and 90 mg for participants > 100 kg, at weeks 0 and 4) in participants with moderate-to-severe plaque psoriasis.[37] These studies also included placebo arms. The primary efficacy endpoint for the comparison of brodalumab to ustekinumab was the PASI 100 response rates at 12 weeks, and the key secondary endpoint was response rates on the PASI 75 at 12 weeks. Other secondary endpoints included the PGA (0 or 1, and 0) response.[37]

For the primary comparative effectiveness endpoint, brodalumab resulted in a higher proportion of participants achieving a PASI 100 response compared with ustekinumab (AMAGINE-2, 44% vs. 22%; $P < .001$; AMAGINE-3, 37% vs. 19%; $P < .001$).[37] In AMAGINE-2, brodalumab 210 mg

did not have significantly greater efficacy in PASI 75 response rate over ustekinumab (86% vs. 70%; *P* = .08), but it did in AMAGINE-3 (85% vs. 69%, *P* = .007).[37] Those treated with brodalumab had significantly greater response when compared with those receiving ustekinumab (AMAGINE-2: 79% vs. 61%; *P* < .001; AMAGINE-3: 80% vs. 57%; *P* < .001) for achieving a 0 or 1 on the PGA.[37] Superiority was also achieved with brodalumab for a PGA score of 0.[37]

In 1 of the newly identified companion studies, authors pooled data from both trials and reported that a higher proportion of participants assigned to brodalumab achieved a PASI 100 (51% vs. 28%; odds ratio [OR] 2.8; 95% CI, 2.1 to 3.7) and PASI 90 (63.1% vs. 42.7%; OR, 2.5; 95% CI, 1.9 to 3.4) response at 52 weeks.[81] In another newly identified companion study, authors reported that a significantly higher proportion of participants assigned to brodalumab achieved a 0 or 1 response on the DLQI at both 12 and 52 weeks.[82] Lastly, authors of 1 of the newly identified companion studies reported results from a post hoc subgroup analysis of efficacy and safety by obesity status.[76] They found no differences in comparative efficacy or safety for participants with a body mass index (BMI) of less than 30 kg/m^2 versus those with BMI of 30 kg/m^2 or more.[76]

Certolizumab vs. Etanercept

We identified 1 new RCT for this update.[15]

CIMPACT was a multicenter, moderate-RoB RCT comparing 2 doses of certolizumab pegol (200 mg or 400 mg) with etanercept in individuals with moderate-to-severe plaque psoriasis.[15] The FDA-approved initial dose and maintenance dose of certolizumab pegol is 400 mg, with maintenance doses of 200 mg advised for participants who weigh less than 90 kilograms.[59] This study also included a placebo arm, and all primary study endpoints were related to the placebo comparisons.[15] Etanercept was administered by unblinded study staff or self-administered, but efficacy assessments were performed by a blinded assessor.[15]

At 12 weeks follow-up, similar proportions of participants achieved a PASI 75 response in the 200-mg (61.3%) and 400-mg (66.7%) dosage groups, but compared with etanercept (53.3%), this finding was only statistically significant for the 400-mg dosage group (calculated RR, 1.2; 95% CI, 0.04 to 1.5).[15] Investigators described similar findings for the proportion achieving a 0 or 1 on the PGA. Authors observed no significant differences on the PASI 90 between either dosage of certolizumab pegol or etanercept.[15]

Etanercept vs. Infliximab

We did not identify any new RCTs for this update.

The previous review included 1 RCT (PIECE) conducted among 50 participants with moderate-to-severe chronic plaque psoriasis.[64] This study randomized participants to 24 weeks of treatment with either etanercept 50 mg twice weekly or infliximab (5 mg/kg intravenously at weeks 0, 2, 6, 14, and 22).[64] We rated this study as high RoB; methodological flaws included insufficient blinding and switching treatments during the primary outcomes follow-up time period. Fewer participants treated with etanercept achieved a PASI 75 response compared with infliximab (35% vs. 72%; *P* = .01).[64] No statistically significant differences were observed for changes in the 36-item Short Form Health Survey (SF-36) Physical Health Component Score (PCS) or Mental Health Component Score (MCS).[64]

Etanercept vs. Ixekizumab

We did not identify any new RCTs for this update.

The previous review included 1 publication reporting on 2 large (> 1,000 participants), phase 3 multicenter, moderate-RoB, randomized trials (UNCOVER-2, UNCOVER-3) comparing etanercept (50 mg twice weekly) with ixekizumab (80 mg twice weekly or 80 mg every 4 weeks, both after an initial starting dose of 160 mg) in participants with moderate-to-severe plaque psoriasis of at least 6 months' duration.[68] This trial also included a placebo arm. [68] Primary efficacy endpoints were the percentage of participants achieving a PGA score of 0 or 1 (with at least a 2-point reduction from baseline at week 12) and a PASI 75 response at 12 weeks.[68] Secondary outcomes included: PGA score of 0; PASI 90; PASI 100; itch Numeric Rating Scale (NRS); and the DLQI.[68] The FDA-approved dose 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.[132]

At 12 weeks, the proportion of participants achieving a PASI 75 response was statistically significantly lower for those randomized to etanercept compared with both doses of ixekizumab (absolute risk difference [ARD] range 31 to 48 percentage points across studies and doses of ixekizumab).[68] Likewise, the percentage of participants achieving a PGA score of 0 or 1 was statistically less in participants randomized to etanercept compared with those randomized to ixekizumab (ARD range 34 to 47 percentage points).[68] The proportion of participants achieving a 0 or 1 on the DLQI was also statistically significantly lower for etanercept compared with either dose of ixekizumab (ARD range 20 to 30 percentage points).[68] Authors observed similar findings on other secondary efficacy outcomes.[68]

Etanercept vs. Secukinumab

We did not identify any new RCTs for this update.

The previous review included 1 moderate-RoB RCT (FIXTURE) comparing etanercept (50 mg twice weekly through week 12, then once weekly) with 2 doses of secukinumab (150 mg and 300 mg, both weekly for 4 weeks, then every 4 weeks) among participants with at least a 6-month history of moderate-to-severe psoriasis.[45] The study's primary endpoints were all placebo comparisons; key secondary outcomes were comparative effectiveness of etanercept compared with secukinumab as assessed by PASI 75 and PGA 0 or 1 response.[45] Both the 150-mg and 300-mg dosages of secukinumab are FDA-approved.[133]

Participants randomized to etanercept achieved a significantly lower response (44%) compared with participants randomized to 300 mg secukinumab (77%) or 150 mg secukinumab (67%; $P < .001$ for both secukinumab doses compared with etanercept).[45] Of those with a PASI 75 response at week 12, a statistically significant higher proportion of participants had a continued response at 52 weeks (73% vs. 84% vs. 82%; $P < .001$ for 300-mg dosage, $P < .009$ for 150-mg dosage).[45] Authors observed similar treatment effects for the PGA 0 or 1 response for both the induction period (through week 12) and the maintenance period (through week 52).[45] Etanercept was also statistically significantly less effective than either dose of secukinumab on the PASI 90 and PASI 100 response.[45] The mean improvement in QoL as measured by the DLQI was numerically lower for participants randomized to etanercept (−7.9) compared with secukinumab 300 mg or 150 mg (−10.4 and −9.7, respectively; *P* value NR).[45]

Etanercept vs. Tofacitinib

We did not identify any new RCTs for this update.

The previous review included 1 moderate-RoB RCT (OPT), published in 2 articles, comparing etanercept (50 mg twice weekly) with 2 doses of tofacitinib (5 mg or 10 mg twice daily).[62,63] Study authors required participants enrolled in this study to have had moderate-to-severe psoriasis for at least 12 months.[62,63] The co-primary efficacy outcomes were the PASI 75 and PGA response at 12 weeks.[62,63] Secondary remission and clinical improvement outcomes included the PASI 90, PASI 50, and the itch severity item score.[62,63] The DLQI and SF-36 were used to assess QoL.[62,63] We note that tofacitinib is not approved for a plaque psoriasis indication; however, it is approved for psoriatic arthritis (at a dose of 5 mg twice daily)[134] so may still be a relevant comparison to consider for this update since individuals with psoriasis may also have psoriatic arthritis.

At 12 weeks, participants randomized to etanercept had a superior response on the PASI 75 (59%) to those randomized to tofacitinib 5 mg (40%; $P < .001$) but a similar response to those randomized to tofacitinib 10 mg (64%; $P = .20$).[62,63] Authors observed similar findings for response on the PGA and on both the PASI 50 and PASI 90.[62,63] Tofacitinib 10 mg was superior to etanercept on the itch severity item score (little or no itch, 57% vs. 69%; $P < .05$).[62,63] The proportion of participants with a 5-point or more improvement on the DLQI was significantly higher for participants randomized to etanercept (75%) compared with tofacitinib 5 mg (66%; $P = .03$) but similar to participants randomized to tofacitinib 10 mg (78%; $P = .31$).[62,63] The mean change in SF-36 PCS and MCS was numerically highest among participants randomized to tofacitinib 10 mg, but study authors did not report statistical significance testing.[62,63]

Etanercept vs. Ustekinumab

We did not identify any new studies for this update.

The previous review included 1 moderate-RoB randomized trial comparing etanercept with ustekinumab in participants with moderate-to-severe plaque psoriasis.[51] Participants were randomized to 3 arms: 50 mg etanercept twice weekly, 45 mg ustekinumab at weeks 0 and 4, or 90 mg ustekinumab at weeks 0 and 4.[51] In this study, participants over 90 kg received the higher dose of ustekinumab (90 mg).[51] The trial lasted 12 weeks, and participants and study personnel administering the drugs were not blinded to treatment allocation.[51] All other study personnel, including assessors and data managers, were blinded to treatment allocation.[51] The FDA-approved dose is 90 mg for persons weighing over 100 kg and 45 mg for persons weighing 100 kg or less.[51]

Significantly fewer participants in the etanercept group achieved the primary outcome (PASI 75 response) compared with both ustekinumab groups (etanercept 50 mg, 57%; ustekinumab 45 mg, 68%; $P = .01$; ustekinumab 90 mg, 74%; $P < .001$).[51] Similarly, statistically significantly fewer participants in the etanercept group demonstrated cleared or minimal disease (0 or 1) on the PGA compared with both ustekinumab groups (etanercept 50 mg, 49%; ustekinumab 45 mg, 65%; $P < .001$; ustekinumab 90 mg, 71%; $P < .001$).[51] Other secondary remission outcomes (PASI 90, PGA 0) had similar findings.[51] No QoL or other efficacy outcomes were reported.

Guselkumab vs. Adalimumab

We did not identify any new studies for this update.

The previous review included 3 moderate-RoB RCTs (X-PLORE,[74] VOYAGE-1,[69,70] VOYAGE-2[71-73]). All 3 RCTs enrolled adults with moderate-to-severe psoriasis for at least 6 months and with at least 10% BSA involvement. [69-74] X-PLORE compared multiple guselkumab doses and dosing intervals to adalimumab (80 mg at week 0, then 40 mg at week 1 and every 2 weeks)[74], whereas VOYAGE-1[69,70] and VOYAGE-2[71-73] compared 100 mg of guselkumab (at weeks 0, 4, and 12) with adalimumab (80 mg at week 0, then 40 mg at week 1 and every 2 weeks). The primary endpoint in X-PLORE was the PGA (0 or 1).[74] No primary endpoints were designated for comparative effectiveness in either VOYAGE trials, but both trials evaluated the PGA (0 or 1), PASI 90, PASI 75, DLQI (0 or 1 and mean change), and change in the Psoriasis Symptoms and Signs Diary (PSSD). [69-73] VOYAGE-2 also reported SF-36 and Hospital Anxiety and Depression Scale (HADS) outcomes.[71-73] The FDA-approved dose of guselkumab is 100 mg at weeks 0, 4, and every 8 weeks thereafter.[135]

For X-PLORE, guselkumab was statistically superior to adalimumab at doses of 50 mg, 100 mg, and 200 mg for the primary endpoint, PGA 0 or 1 (58% adalimumab vs. 86% guselkumab 100 mg).[74] However, no statistical differences were observed between groups for secondary endpoints (PASI 75, DLQI).[74] For both VOYAGE trials, guselkumab was statistically superior to adalimumab on all PGA and PASI outcomes, the DLQI, and the PSSD.[69-73] The authors of VOYAGE-2 reported statistically significant larger improvements for guselkumab for the SF-36 PCS and HADS anxiety scale compared with adalimumab, but no statistical differences for the SF-36 MCS and the HADS depression scale.[71-73]

Guselkumab vs. Secukinumab

We did not identify any new studies for this update; however, we did identify 1 new companion article[80] to the previously included RCT.[44]

The previous review included 1 moderate-RoB RCT (ECLIPSE) comparing 100 mg of guselkumab (at weeks 0, 4, and 12, then every 8 weeks) with 300 mg of secukinumab (at weeks 0, 1, 2, 3, and 4, then every 4 weeks) among participants who had had moderate-to-severe plaque psoriasis for at least 6 months.[44] The primary study endpoint was PASI 90 response at week 48. Secondary remission outcomes include PASI 75 response at combined week 12 and week 48 endpoint, PASI 75 response at week 12, PASI 100 response at week 48, and IGA 0 and 0 or 1 response at week 48. [44]

At week 48, guselkumab was superior to secukinumab for achieving a PASI 90 response (84% vs. 70%; $P < .001$).[44] Guselkumab was noninferior to secukinumab for achieving a PASI 75 response at combined week 12 and week 48 endpoint (85% vs. 80%; noninferiority $P < .001$; superiority $P = .06$).[44] Per the study's prespecified analysis plan, no further secondary endpoints were subjected to statistical significance testing once a nonsignificant finding for superiority or noninferiority was reached.[44] Guselkumab was numerically superior to secukinumab on the PASI 100 and IGA 0 and 0 or 1 response at week 48, whereas secukinumab was numerically superior to guselkumab on the PASI 90 and PASI 75 response at week 12.[44] The newly identified companion article reported findings from subgroup analyses based on age, weight, BMI, severity of disease, body area affected, and prior medication, and found guselkumab remained more

effective than secukinumab in each strata of subgroups evaluated.[80] In other words, there was no effect modification based on any population characteristic evaluated.

Ixekizumab vs. Guselkumab

We identified 1 new moderate-RoB RCT for this update.[17,36]

The IXORA-R study was a multicenter RCT comparing ixekizumab 80 mg every 2 weeks and then every 4 weeks to guselkumab 100 mg at weeks 0, 4, 12, and 20, in adults who had had moderate-to-severe plaque psoriasis for at least 6 months.[17] The primary study endpoint was PASI 100 response at 12 weeks. Other outcomes were reported at both 12-weeks and 24-weeks follow-up.[17,36] The FDA recommended dosage is 160 mg at week 0 followed by 80 mg every 4 weeks.

At week 12, a higher proportion of individuals assigned to ixekizumab achieved a PASI 100 response (41%) compared with guselkumab (25%; calculated RR, 1.7; 95% CI, 1.4 to 2.0).[17] A similar response was seen on the Static Physicians Global Assessment (sPGA), DLQI, and Patient's Global Assessment (PtGA) measures.[17] At week 24, the PASI 100 responses were similar between groups (50% ixekizumab, 52% guselkumab; calculated RR, 0.96; 95% CI, 0.85 to 1.10).[36] Further, no significant differences in other measures (PASI 50, 75, and 90; PtGA, sPGA, DLQI, itch NRS) were observed at 24 weeks.[36]

Ixekizumab vs. Secukinumab

We identified 1 new moderate-RoB RCT for this update.[23]

This study was conducted at a single hospital in Kuwait and enrolled only 54 participants with moderate-to-severe plaque psoriasis with genital lesions for at least 6 months.[23] Authors compared ixekizumab 80 mg every 2 weeks and then 4 weeks, after an initial loading dose of 160 mg, with secukinumab 300 mg weekly for 4 weeks and then every 4 weeks. Study endpoints included overall measures of improvement and the genital psoriasis symptom score (GPSS).[23]

At week 24, the proportion reporting a 0 or 1 on sPGA was similar (ixekizumab, 85.7%; secukinumab, 84.6%; calculated RR, 1.01; 95% CI, 0.81 to 1.30).[23] Similarly, the proportion reporting at least a 3-point improvement on the GPSS was similar (69.7% vs. 68.3%; calculated RR, 1.03; 95% CI, 0.73 to 1.50), and the proportion reporting impaired sexual functioning between groups was also not statistically significantly different.[23]

Ixekizumab vs. Ustekinumab

We did not identify any new RCTs for this update; however, we did identify 2 new companion articles[79,83] providing longer-term outcomes for an RCT (IXORA-S) included in the previous review.[47,48]

The previously included moderate-RoB RCT compared ixekizumab 80 mg (every 2 weeks through week 12, then every 4 weeks) with ustekinumab (45 mg or 90 mg depending on body weight, at weeks 0, 4, and 16) among adults who had had moderate-to-severe psoriasis for at least 6 months, and reported outcomes after a 12-week induction period[47] and after a 52-week maintenance period.[48] The primary efficacy endpoint was the PASI 90 at 12 weeks. Secondary remission and clinical improvement outcomes included the PASI 75, PASI 100, PGA, itch NRS,

and skin pain as assessed with a visual analog scale (VAS). Study authors assessed QoL with the DLQI.[47,48] The FDA-approved dose 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.[132]

At 12 weeks, participants randomized to ixekizumab had a superior response on the PASI 90 (73%) compared with participants randomized to ustekinumab (42%; *P* < .001).[47,48] A similar treatment effect was observed for response on the PASI 75, PASI 100, and PGA.[47,48] Changes on the itch NRS and skin pain VAS were numerically higher for ixekizumab but were not statistically different from scores for ustekinumab.[47,48] Sixty-one percent of participants randomized to ixekizumab reported no or minimal impact of condition on the QoL (DLQI 0 or 1) compared with 45% of participants randomized to ustekinumab (*P* = .01).[47,48] Participants randomized to ixekizumab continued to have larger clinical improvement and disease remission outcomes compared with participants randomized to ustekinumab after 24 and 52 weeks.[48,83] One of the newly identified companion articles reported general health-related QoL measures including the EuroQol 5-item (EQ-5D), visual analog scale (EQ-VAS), psoriasis-specific EQ-5D (EQ-PsO), and SF-36 PCS and MCS.[83] Across these measures, participants assigned to ixekizumab had larger improvements, but only some of these findings were statistically signficant.[83] The other newly identified companion study reported outcomes for the subset of participants with nail psoriasis.[79] A significantly higher proportion of participants assigned to ixekizumab achieved complete remission as measured by the Nail Psoriasis Area and Severity Index (NAPSI) at 16 weeks (31% vs. 16.2%; *P* = .02) and at 52 weeks (62% vs. 29%; *P* < .001).[79]

Risankizumab vs. Adalimumab

We did not identify any new RCTs for this update.

The previous review included 1 moderate-RoB RCT (IMMVENT).[46] This multicenter, phase 3 RCT compared 150 mg of risankizumab (at weeks 0 and 4) with 40 mg adalimumab (80 mg at week 0, then 40 mg every other week) over 16 weeks among participants with moderate-to-severe chronic plaque psoriasis.[46] The co-primary endpoints were PASI 90 response and PGA 0 or 1 at 16 weeks.[46] Secondary remission endpoints included the PASI 75 and PASI 100 response and PGA 0 response.[46] The study authors assessed QoL with the DLQI 0 or 1 response, and also assessed work-related functioning with the work limitations questionnaire (WLQ).[46]

At 16 weeks, risankizumab was superior to adalimumab on the PASI 90 response (ARD, 25%; 95% CI, 18% to 32%; *P* < .001).[46] A similar finding was observed for the PGA 0 or 1 response and on all secondary remission outcomes.[46] For QoL, 66% of participants randomized to risankizumab achieved a 0 or 1 response on the DLQI compared with 49% of participants randomized to adalimumab (*P* < .001).[46] Participants randomized to risankizumab also had a larger improvement (mean −2.8) on the WLQ compared with participants randomized to adalimumab (mean −1.9, *P* = .01).[46]

Risankizumab vs. Secukinumab

We identified 1 new RCT for this update.[19]

The IMMerge multicenter, moderate-RoB RCT randomized participants with moderate-to-severe chronic plaque psoriasis with or without psoriatic arthritis to risankizumab 150 mg at weeks 0 and 4 then every 12 weeks, or secukinumab 300 mg weekly for the first 4 weeks then every 4

weeks thereafter.[19] The primary study endpoints were noninferiority of the PASI 90 response at 16 weeks and superiority of the PASI 90 at week 52. The authors also reported additional secondary outcomes.[19]

At week 16, risankizumab was noninferior (within the 12% ARD margin) to secukinumab on the PASI 90 (risankizumab 73.8% vs. secukinumab 65.6; ARD, 8.2%; 95% CI −2.2 to 18.6).[19] At week 52, a higher proportion of participants assigned to risankizumab achieved a PASI 90 response (86.6%) compared with secukinumab (57.1%; ARD, 29.8; 95% CI, 20.8 to 38.8).[19] The authors observed similar outcomes at 52 weeks on the PASI 100, PASI 75, and sPGA 0 or 1 measures.[19]

Risankizumab vs. Ustekinumab

We did not identify any new studies for this update; however, we did identify 1 new companion article[78] to 2 of the previously included studies.[67]

The previous review included 3 RCTs (UltIMMA-1 and UltIMMA-2[67] and Papp et al.[52]); we rated all as moderate RoB. UltIMMA-1 and UltIMMA-2 were multicenter phase 3 trials that enrolled adults who have had moderate-to-severe plaque psoriasis for at least 6 months and randomized them to either 150 mg of risankizumab (at weeks 0 and 4, then every 12 weeks) or 45 mg or 90 mg (depending on body weight) of ustekinumab (at weeks 0 and 4, then every 12 weeks).[67] These RCTs also included a placebo arm.[67] The co-primary endpoints were PASI 90 and PGA (0 or 1) response at 16 weeks; both studies also reported outcomes at 52 weeks.[67]

At 16 weeks, more participants randomized to risankizumab in UltIMMA-1 and UltIMMA-2 had disease remission compared with ustekinumab (PASI 90 75% vs. 42%; $P < .001$ in UltIMMA-1; 75% vs. 48%; $P < .001$ in UltIMMA-2).[67] Authors observed a similar treatment effect for the PGA (0 or 1, and 0 only), PASI 100, and Psoriasis Symptom Scale (PSS).[67] Participants randomized to risankizumab also demonstrated a larger improvement in QoL (DLQI 0 or 1 response, 66% vs. 43%; $P < .001$ in UltIMMA-1; 67% vs. 47%; $P < .001$ in UltIMMA-2).[67] In the newly identified companion article, authors reported QoL measures (EQ-5D); risankizumab was significantly more effective at improving QoL compared with ustekinumab at 16 and 52 weeks.[78]

The multicenter RCT conducted by Papp and colleagues compared several dose regimens of risankizumab (single 18-mg dose, 90 mg or 180 mg at weeks 0, 4, and 16) with ustekinumab (45 mg or 90 mg depending on body weight at weeks 0, 4, and 16) in participants who had had moderate-to-severe plaque psoriasis for at least 6 months.[52] We rated this study as moderate RoB because of unclear allocation and insufficient blinding in addition to extensive manufacturer involvement in study design, execution, and reporting. In this RCT, risankizumab (data pooled for 90-mg and 180-mg dosages) was more effective than ustekinumab for the PASI 90 response (77% vs. 40%; $P < .001$).[52] Authors observed similar treatment effects for the PASI 50, PASI 75, PASI 100, and PGA response.[52] Participants randomized to either the 90-mg or 180-mg dosage of risankizumab saw larger improvements in QoL (DLQI 0 or 1, 72% vs. 53%; $P < .001$).[52]

Secukinumab vs. Ustekinumab

We did not identify any new RCTs for this update; however, we did identify 1 new companion article[77] for 1 of the previously included RCTs.[39]

The previous review included 2 moderate RoB RCTs (CLARITY[39] and CLEAR[40-42]). Both compared secukinumab 300 mg (at week 0, 1, 2, and 3, then every 4 weeks) with ustekinumab (45 mg or 90 mg depending on body weight at weeks 0 and 4, then every 12 weeks) in persons with chronic moderate-to-severe psoriasis.[39-42] Study authors reported results for CLEAR at 16 weeks and 52 weeks follow-up.[40-42] The primary study endpoint in CLEAR was the PASI 90 at 16 weeks; additional remission and clinical improvement outcomes included the PASI 75, PASI 100, IGA, and symptom scores (pain, itch, and scaling).[40-42] The DLQI and EQ-5D instrument were used to assess QoL, and the Work Productivity and Activity Impairment Questionnaire-Psoriasis (WPAI-PSO) was used to assess work-related disability.[40-42] The co-primary endpoints in CLARITY were the PASI 90 and IGA 0 or 1 response at 12 weeks; secondary outcomes included the PASI 75 and PASI 100 at 12 weeks and 16 weeks, the IGA 0 or 1 response at 16 weeks, and the DLQI at 12 weeks and 16 weeks.[39] We identified a new companion study for CLARITY reporting outcomes at 52 weeks.[77]

In CLEAR and CLARITY, secukinumab was superior to ustekinumab. For the primary study outcome in CLEAR, participants randomized to secukinumab had a higher PASI 90 response (79%) compared with those randomized to ustekinumab (58%; $P < .001$) at 16 weeks.[40] Secukinumab was superior to ustekinumab on all secondary remission and clinical improvement outcomes.[40] Secukinumab was also superior to ustekinumab for improving QoL (DLQI 0 or 1, 72% vs. 57%; $P < .001$) at 16 weeks.[40] At 52 weeks in CLEAR, secukinumab remained superior to ustekinumab on the PASI 90 response (75% vs. 61%; $P < .001$) and on all secondary remission, clinical improvement, and QoL outcomes.[41] For the primary study outcome in CLARITY at 12 weeks, participants randomized to secukinumab had a higher PASI 90 response (67%) compared with those randomized to ustekinumab (48%; $P < .001$).[39] Authors saw similar treatment effects on the IGA 0 or 1 response, and on the PASI 75 and PASI 100 at both 12 and 16 weeks.[39] Participants randomized to secukinumab also had greater improvements in QoL (DLQI 0 or 1, 68%) compared with ustekinumab (56%; $P < .001$).[39] Secukinumab remained superior to ustekinumab at 52 weeks in CLARITY as well.[77] For example, 73.2% of participants assigned to secukinumab maintained a PASI 90 response, while 59.8% of those assigned to ustekinumab maintained a PASI 90 response (OR, 1.84; 95% CI, 1.41 to 2.41).[77] Authors observed similar findings for the PASI 75, PASI 100, IGA 0 or 1, and DLQI 0 or 1 outcomes at 52 weeks.[77]

Tildrakizumab vs. Etanercept

We did not identify any new studies for this update; however, we identified 1 new companion article[75] to the previously included study for this comparison.[65]

The previously included moderate-RoB RCT (RESURFACE-2) compared tildrakizumab (100 mg or 200 mg at week 0 and week 4, then every 12 weeks) with etanercept (50 mg twice weekly through week 12, then once weekly) in adults with moderate-to-severe plaque psoriasis.[65] This trial also included a placebo study group.[65] The co-primary study endpoints were the PASI 75 and PGA 0 or 1 response at 12 weeks.[65] Secondary remission and improvement outcomes included the PASI 90 and 100 at 12 and 28 weeks, the PASI 75, and PGA 0 or 1 at 28 weeks.[65] QoL was assessed with the DLQI at 12 and 28 weeks.[65] The FDA-approved dose for tildrakizumab is 100 mg at weeks 0 and 4, then every 12 weeks.

Participants randomized to etanercept had an inferior PASI 75 response at week 12 (48%) compared with participants randomized to either doses of tildrakizumab (100 mg, 61%; *P* = .001; 200 mg, 66%; *P* < .001).[65] Authors observed a similar treatment effect for the PGA 0 or 1, PASI 90, and PASI 100 response at week 12.[65] Etanercept remained inferior to both doses of tildrakizumab at 28 weeks on all remission outcomes.[65] For QoL, at 12 weeks, etanercept was inferior to 200 mg tildrakizumab; 36% of participants randomized to etanercept achieved a 0 or 1 response on the DLQI compared with 47% in the 200-mg dosage group (*P* = .003).[65] Forty percent of participants randomized to 100 mg of tildrakizumab achieved a DLQI 0 or 1 response, which was not statistically different from the response in etanercept (*P* = .22).[65] However etanercept was inferior to both dosages at 28 weeks follow-up (39% vs. 54% vs. 65%; *P* < .001 for both dosages compared with etanercept).[65] Authors of the newly identified companion study reported a subgroup analysis of efficacy based on metabolic syndrome status; they observed no differences in efficacy between those with and without metabolic syndrome.[75]

Table 3. Evidence Table for Efficacy Outcomes in Adults for TIMs for Plaque Psoriasis (Brief Version)

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Apremilast vs. etanercept								
Reich et al., 2017[49] LIBERATE	250	16 weeks	Apremilast 30 mg twice per day vs. etanercept 50 mg once weekly	PASI 75	PGA, BSA, PASI 50, DLQI	Adults with moderate-to-severe plaque psoriasis ≥ 12 months' duration and involving ≥ 10% BSA	No statistically significant difference between groups	Moderate
Brodalumab vs. ustekinumab								
Lebwohl et al., 2015[37] Hsu et al., 2020[76] Lambert et al., 2021[82] Warren et al., 2021[81] AMAGINE-2, AMAGINE-3	1,831 and 1,881	12 weeks	Brodalumab 210 mg at weeks 0, 1, 2 then every 2 weeks vs. ustekinumab 45 mg or 90 mg[a] at weeks 0 and 4	PASI 75, PGA 0 or 1, PASI 100	PASI 100, PGA 0	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA	Brodalumab was more effective than ustekinumab	Moderate
Certolizumab pegol vs. etanercept								
Lebwohl et al., 2018[15] CIMPACT	502 (without the placebo arm)	12 weeks	Certolizumab pegol 200 mg every 2 weeks vs. certolizumab pegol 400 mg every 2 weeks vs. etanercept 50 mg twice weekly	NA because all primary study endpoints were placebo comparisons	PASI 75, PASI 90, PGA 0 or 1	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Certolizumab pegol 400 mg (but not 200 mg) was more effective than etanercept on 2 of 3 measures reported	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Etanercept vs. infliximab								
De Vries et al., 2017[64] PIECE	50	24 weeks	Etanercept 50 mg twice weekly vs. infliximab 5 mg/kg at weeks 0, 2, 6, 14, 22	PASI 75	PASI 75 at week 6 and 12, IGA, Skindex-17, SF-36	Adults with plaque psoriasis with PASI ≥ 10, BSA ≥ 10 and/or PASI ≥ 8 plus Skindex-29 ≥ 35	Infliximab was more effective than etanercept	High
Etanercept vs. ixekizumab								
Griffiths et al., 2015[68] UNCOVER-2, UNCOVER-3	1,224 and 1,346	12 weeks	Etanercept 50 mg twice weekly vs. ixekizumab 80 mg every 2 weeks[b] vs. ixekizumab 80 mg every 4 weeks[b]	PASI 75, PGA 0 or 1	PGA 0, PASI 90, PASI 100, NRS, DLQI	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA	Ixekizumab was more effective than etanercept	Moderate
Etanercept vs. secukinumab								
Langley et al., 2014[45] FIXTURE	1,306	52 weeks	Etanercept 50 mg twice weekly vs. secukinumab 300 mg or 150 mg weekly for 4 weeks then every 4 weeks	NA[c]	PASI 75, PGA, PASI 90, PASI 100, PASI 50, DLQI	Adults with plaque psoriasis of ≥6 months' duration, poorly controlled with current therapies and involving at least 10% BSA	Secukinumab was more effective than etanercept	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Etanercept vs. tofacitinib								
Bachelez et al., 2015[62] Valenzuela et al., 2016[63] OPT	1,106	12 weeks	Etanercept 50 mg twice weekly vs. tofacitinib 10 and 5 mg twice daily[d]	PASI 75, PGA	PASI 90, PASI 50, itch severity item score, DLQI, SF-36	Adults with plaque psoriasis of ≥ 12 months' duration, poorly controlled with current therapies and involving at least 10% BSA	Etanercept was more effective than 5 mg twice daily but similar to 10 mg twice daily	Moderate
Etanercept vs. ustekinumab								
Griffiths et al., 2010[51]	903	12 weeks	Etanercept 50 mg twice weekly vs. ustekinumab 45 mg and 90 mg at weeks 0 and 4	PASI 75	PGA, PASI 90	Adults with plaque psoriasis of at least 6 months' duration and involving > 10% BSA	Etanercept was less effective than ustekinumab	Moderate
Guselkumab vs. adalimumab								
Gordon et al., 2015[74] X-PLORE	251 (without the placebo arm)	16 weeks	Adalimumab 40 mg every 2 weeks[e] vs. guselkumab 5 mg, 15 mg, 50 mg, 100 mg, 200 mg[f]	PGA 0 or 1	PASI 75, DLQI	Adults with moderate-to-severe plaque psoriasis for at least 6 months and involving ≥ 10% BSA	Guselkumab was more effective than adalimumab on primary endpoint at doses of 50 mg, 100 mg, and 200 mg but no significant differences on secondary endpoints at same doses	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Blauvelt et al., 2017[69] Papp et al., 2018[70] VOYAGE-1	663 (without the placebo arm)	16 weeks	Adalimumab 40 mg every 2 weeks[e] vs. guselkumab 100 mg at weeks 0, 4, and 12	No primary endpoints specified	IGA 0 or 1, IGA 0, PASI 90, PASI 75, PASI 100, DLQI, PSSD	Adults with moderate-to-severe psoriasis for ≥ 6 months and involving ≥ 10% BSA	Guselkumab was more effective than adalimumab on all outcomes	Moderate
Reich et al., 2017[73] Reich et al., 2019[71] Gordon et al., 2018[72] VOYAGE-2	744 (without the placebo arm)	16 weeks	Adalimumab 40 mg every 2 weeks[e] vs. guselkumab 100 mg at weeks 0, 4 and 12	No primary endpoints specified	IGA 0, IGA 0 or 1, PASI 90, PASI 75, Change in DLQI, change in PSSD score	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA	Guselkumab was more effective than adalimumab on all psoriasis-specific outcomes, SF-36 PCS, and HADS-A, but similar on SF-36 MCS and HADS-D	Moderate
Guselkumab vs. secukinumab								
Reich et al., 2019[44] Blauvelt et al., 2021[80] ECLIPSE[44]	1,048	48 weeks	Guselkumab 100 mg at weeks 0, 4, 12 then every 8 weeks vs. secukinumab 300 mg at weeks 0, 1, 2, 3, 4 then every 4 weeks	PASI 90 at week 48	PASI 75 at week 12 and 48, PASI 90, PASI 100, IGA 0, IGA 0 or 1	Adults with moderate-to-severe psoriasis with BSA ≥ 10%, for ≥ 6 months	Guselkumab was more effective for primary endpoint and was noninferior for the first secondary end point[g] Mixed results on other endpoints	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Ixekizumab vs. guselkumab								
Blauvelt et al., 2020[17] Blauvelt et al., 2021[36] IXORA-R	1,027	24 weeks	Ixekizumab 80 mg every 2 weeks then every 4 weeks vs. guselkumab 100 mg at weeks 0, 4, 12, and 20	PASI 100	sPGA 0, PtGA 0 or 1, DLQI, itch NRS	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Ixekizumab more effective than guselkumab at week 12 but no difference by week 24; faster time to skin clearance with ixekizumab vs. guselkumab	Moderate
Ixekizumab vs. secukinumab								
Al Mutairi et al., 2020[23]	54	24 weeks	Ixekizumab 80 mg every 2 weeks vs. secukinumab 300 mg every 4 weeks	NR	sPGA 0 or 1, sPGA 0, GPSS, MGH-SFQ	Adults with moderate-to-severe plaque psoriasis for at least 6 months with BSA ≥ 10%. with genital involvement	No significant differences between Ixekizumab and secukinumab on all measures reported	Moderate
Ixekizumab vs. ustekinumab								
Reich et al., 2017[47] Paul et al., 2018[48] Wasel et al., 2020[79] Puig et al., 2020[83,136] IXORA-S	302	52 weeks	Ixekizumab 80 mg every 2 weeks through week 12 then every 4 weeks vs. ustekinumab 45 or 90 mg[a] at weeks 0, 4 and 16	PASI 90	PASI 75, PASI 100, PGA, DLQI, itch NRS, skin pain, EQ-5D-5L, SF-36	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration, and PASI ≥10	Ixekizumab was more effective than ustekinumab on all outcomes but itch NRS and skin pain at 12 weeks and 52 weeks	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Risankizumab vs. adalimumab								
Reich et al., 2019[46] IMMVENT	605	16 weeks	Risankizumab 150 mg at week 0 and 4 vs. adalimumab 40 mg every 2 weeks[e]	PASI 90, PGA 0 or 1	PASI 75, PASI 100, PASI 50, DLQI, WLQ	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and involving ≥ 10% BSA	Risankizumab was more effective than adalimumab on all primary and secondary outcomes	Moderate
Risankizumab vs. secukinumab								
Warren et al., 2021[19] IMMerge	327	52 weeks	Risankiz-umab 150 mg every 12 weeks vs. secukinumab 300 mg every 4 weeks	PASI 90	PASI 100, sPGA 0/1, PASI 75	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA	Risankizumab was more effective than secukinumab on primary and secondary outcomes	Moderate
Risankizumab vs. ustekinumab								
Papp et al., 2017[52]	166	48 weeks	Risankizumab 90 and 180 mg[h] at weeks 0, 4 and 16 vs. ustekinumab 45 or 90 mg[a] at weeks 0, 4 and 16	PASI 90	PASI 50, PASI 75, PASI 100, PGA, NAPSI, PGAR, PAI, EQ-5D, DLQI	Adults with stable moderate-to-severe plaque psoriasis ≥ 6 months, ≥ 10% BSA, and PASI ≥ 12	Risankizumab was more effective than ustekinumab	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Gordon et al., 2018[67,78] UltIMMA-1	506	52 weeks	Risankizumab 150 mg at week 0, 4 then every 12 weeks vs. ustekinumab 45 mg or 90 mg[a] at weeks 0, 4, then every 12 weeks	PASI 90, PGA 0 or 1	PGA 0, PASI 100, DLQI 0 or 1, PSS 0, PASI 75, PSS score, EQ-5D	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and involving at least 10% BSA	Risankizumab was more effective than ustekinumab on primary and nearly all secondary endpoints	Moderate
Gordon et al., 2018[67,78] UltIMMA-2	393	52 weeks	Risankizumab 150 mg at week 0, 4 then every 12 weeks vs. ustekinumab 45 mg or 90 mg[a] at weeks 0, 4, then every 12 weeks	PASI 90, PGA 0 or 1	PGA 0, PASI 100, DLQI 0 or 1, PSS 0, PASI 75, PSS score, EQ-5D	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and involving ≥ 10% BSA	Risankizumab was more effective than ustekinumab on primary endpoint and nearly all secondary endpoints	Moderate
Secukinumab vs. ustekinumab								
Blauvelt et al., 2017[41,42] Thaci et al., 2015[40] CLEAR	676	52 weeks	Secukinumab 300 mg at weeks 0, 1, 2, 3, then every 4 weeks vs. ustekinumab 45 or 90 mg[a] at week 0, 4, then every 12 weeks	PASI 90 at 16 weeks	PASI 75, PASI 100, IGA, DLQI, EQ-5D-3L, WPAI-PSO, HAQ-DI, pain, itch scaling	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and ≥ 10% BSA	Secukinumab was more effective than ustekinumab at both 16 and 52 weeks	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Bagel et al., 2018[39] and 2021[77] CLARITY	1,102	52 weeks	Secukinumab 300 mg at weeks 0, 1, 2, 3, then every 4 weeks vs. ustekinumab 45 mg or 90 mg[a] at weeks 0, 4, then every 12 weeks	PASI 90, IGA 0 or 1	PASI 75, PASI 90, PASI 100, IGA 0 or 1, DLQI 0 or 1	Adults with moderate-to-severe plaque psoriasis and involving ≥ 10% BSA	Secukinumab was more effective than ustekinumab on all outcomes at both 16 and 52 weeks	Moderate
Tildrakizumab vs. etanercept								
Reich et al., 2017[65] reSURFACE 2	934 (without the placebo arm)	28 weeks	Etanercept 50 mg twice weekly vs. tildrakizumab 100 mg and 200 mg at weeks 0 and 4 then every 12 weeks	PASI 75, PGA 0 or 1, both at 12 weeks	PASI 90, PASI 100, DLQI at 12 weeks, PASI and DLQI at 28 weeks	Adults with moderate-to-severe plaque psoriasis involving ≥ 10% BSA	Tildrakizumab was more effective than etanercept on all primary and nearly all secondary outcomes	
Bimekizumab (pipeline drug) vs. adalimumab								
Warren et al., 2021[25] BE SURE	478	24 weeks	Bimekizumab 320 mg every 4 weeks vs. bimekizumab 320 mg every 4 weeks then every 8 weeks vs. adalimumab 40 mg every 2 weeks	PASI 90 and IGA 0 or 1	PASI 100, PASI 75, DLQI	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving 10% BSA	Bimekizumab was more effective than adalimumab on all measures reported	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Bimekizumab (pipeline drug) vs. placebo								
Papp et al., 2018[38] BE ABLE	250	12 weeks	Bimekizumab 64 mg, 160 mg, 160 mg with 320 mg loading dose, 320 mg, 480 mg, all every 4 weeks vs. placebo every 4 weeks	PASI 90 at week 12	PASI 90 at week 8, PASI 75 and PASI 100 at week 12, IGA 0 or 1 at weeks 8 and 12	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and involving ≥ 10% BSA	Bimekizumab was more effective than placebo at all doses evaluated for all primary and secondary outcomes	Moderate
Gordon et al., 2021[22] BE READY	435	16 weeks	Bimekizumab 320 mg every 4 weeks vs. placebo	PASI 90 and IGA 0 or 1	PASI 100, IGA 0, P-SIM, DLQI 0/1	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Bimekizumab was more effective than placebo on all measures reported	Moderate
Glatt et al., 2017[53]	39	One infusion, 20 weeks follow-up	Bimekizumab 8 mg, 40 mg, 160 mg, 480 mg, or 640 mg as a single dose vs. placebo	Adverse events	LSS, PASI, PGA 0 or 1	Adults with plaque psoriasis ≥ 6 months and involving ≥ 5% BSA	Bimekizumab demonstrated dose dependent improvement in all clinical outcomes vs. placebo for the 160 mg and higher doses.	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Reich et al., 2021[21] BE VIVID	567	52 weeks	Bimekizumab 320 mg vs. placebo	PASI 90 and IGA 0 or 1	PASI 100, IGA 0, PASI 75, scalp IGA, P-SIM	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Bimekizumab was more effective than placebo on all primary and secondary outcomes	Moderate
Bimekizumab (pipeline drug) vs. secukinumab								
Reich et al., 2021[24] BE RADIANT	743	48 weeks	Bimekizumab 320 mg every 4 weeks then every 4 or 8 weeks vs. secukinumab 300 mg every 4 weeks	PASI 100	PASI 90, PASI 75, IGA 0 or 1	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Bimekizumab was more effective than secukinumab at week 16, and both doses evaluated for maintenance were more effective than secukinumab at week 48	Moderate
Bimekizumab (pipeline drug) vs. ustekinumab								
Reich et al., 2021[21] BE VIVID	567	52 weeks	Bimekizumab 320 mg vs. ustekinumab 45 mg or 90 mg	PASI 90 and IGA 0 or 1	PASI 100, IGA 0, PASI 75, scalp IGA, P-SIM	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration and involving ≥ 10% BSA	Bimekizumab was more effective than ustekinumab on all primary and secondary outcomes	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Deucravacitinib (pipeline drug) vs. placebo								
Papp et al., 2018[54]	268	12 weeks	BMS-986165 3 mg every other day, daily, twice daily, 6 mg twice daily, or 12 mg daily vs. placebo	PASI 75	PASI 50, PASI 90, PASI 100, PGA 0 or 1, DLQI 0 or 1	Adults with moderate-to-severe plaque psoriasis ≥ 6 months and involving ≥ 10% BSA	All doses 3 mg twice daily or greater were more effective than placebo on nearly all outcomes	Moderate

Notes. [a] Dose depending on body weight, 45 mg if ≤ 100 kg and 90 mg if > 100 kg. [b] The FDA-approved dose for this agent is an initial 160-mg dosage, then 80 mg at weeks 2, 4, 6, 8, 10, 12, then every 4 weeks. [c] All primary study endpoints were placebo comparisons. [d] The FDA-approved dosage for this agent is 5 mg twice daily. [e] After initial dose of 80 mg and dose of 40 mg at week 1. [f] Dosing intervals varied by dose, doses administered either at weeks 0 and 4 then every 12 weeks or at week 0 and every 8 weeks. [g] No statistical testing done on other secondary time points because of hierarchical analysis, but guselkumab was numerically more effective for the 3 endpoints at week 48, and secukinumab was numerically more effective for the 2 endpoints at week 12. [h] A single 18-mg dosage group was also included in this study.

Abbreviations. BSA: body surface area; DLQI: Dermatology Life Quality Index; EQ-5D-3L or 5L: European QoL 5-Dimension Health Questionnaire, 3-level version or 5-level version; FDA: US Food and Drug Administration; GPSS: Genital Psoriasis Symptom Scale; HADS-D/HADS-A: Hospital Anxiety or Depression Scale; HAQ-DI: Health Assessment Questionnaire–Disability Index; IGA: Investigator Global Assessment; kg: kilogram; LSS: lesion severity score; mg: milligram; MGH-SFQ: Massachusetts General Hospital-Sexual Functioning Questionnaire; NA: not applicable; NAPSI: Nail Psoriasis Severity Index; NR: not reported; NRS: Numeric Rating Scale; PAI: patient's assessment of itching; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PGA: Physician Global Assessment; PGAR: Patient's Global Assessment Rank; P-SIM: Psoriasis Symptoms and Impacts Measure; PSS: Psoriasis Symptom Scale; PSSD: Psoriasis Symptoms and Signs Diary; PtGA: Patient's Global Assessment; SF-36: 36-item Short Form Health Survey; SF-36 MCS: 36-item Short Form Health Survey Mental Health Component Score; SF-36 PCS: 36-item Short Form Health Survey Physical Health Component Score; sPGA: Static Physicians Global Assessment; TIM: targeted immune modulator; vs.: versus; WLQ: Work Limitations Questionnaire; WPAI-PSO: Work Productivity and Activity Impairment Questionnaire-Psoriasis.

Comparative Harms (KQ2)

In this section, we describe harm findings for the 25 included RCTs described for KQ1, plus 10 additional cohort studies reporting on eligible harms.[27-32,55,57-59] Appendix B, Tables B1 and B2 provide detailed study characteristics and results from the included RCTs, and Table B3 provides detailed study characteristics and results from the included cohort studies.

Harms Reported in RCTs

Table 4 summarizes high-level findings for harms from included RCTs that evaluated 18 different head-to-head comparisons; detailed findings are summarized in Table 5. Overall, we observed few differences in harms for TIMs in head-to-head comparisons.

Table 4. Summary of RCTs of AEs in Adults Receiving TIMs for Plaque Psoriasis

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Apremilast vs. etanercept				
Reich et al., 2017[49] LIBERATE	250	16 weeks	Lower risk of AEs for etanercept than apremilast (53% vs. 71%; RR, 0.75; 95% CI, 0.58 to 0.95). No significant differences in SAEs or withdrawals due to AEs.	Moderate
Brodalumab vs. ustekinumab				
Lebwohl et al., 2015[37] AMAGINE-2	1,831	52 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Lebwohl et al., 2015[37] AMAGINE-3	1,881	52 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Certolizumab pegol vs. etanercept				
Lebwohl et al., 2018[15] CIMPACT	502 (without the placebo arm)	12 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Etanercept vs. infliximab				
De Vries et al., 2017[64] PIECE	48	24 weeks	No significant differences in AEs, SAEs, withdrawals due to AEs, or injection-site reactions.	High
Etanercept vs. ixekizumab				
Griffiths et al., 2015[68] UNCOVER-2 UNCOVER-3	2,570	12 weeks	No significant differences in AEs, SAEs, withdrawals due to AEs, or injection-site reactions.	Moderate
Etanercept vs. secukinumab				
Langley et al., 2014[45] FIXTURE	1,306	52 weeks	Higher risk of injection-site reactions for etanercept than secukinumab 300-mg dose (11% vs. 1%; RR, 14.9; 95% CI, 6.7 to 33.2). No significant differences in AEs, SAEs or withdrawals due to AEs.	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Etanercept vs. tofacitinib				
Bachelez et al., 2015[62] Valenzuela et al., 2016[63] OPT	1,106	12 weeks	Higher incidence of withdrawal due to AEs for etanercept than tofacitinib 5 mg twice daily (3% vs. 1%; RR, 3.6; 95% CI, 1.01 to 12.8). No significant difference in AEs, SAEs for either the 5 mg twice daily or 10 mg twice daily doses. No significant difference in withdrawals due to AEs for etanercept vs. the 10 mg twice daily dose.	Moderate
Etanercept vs. ustekinumab				
Griffiths, et al., 2010[51]	903	12 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs. Injection-site reactions more frequent with etanercept than ustekinumab (RR, 6.3; 95% CI, 4 to 9.8), but those participants received more injections than the ustekinumab groups.	Moderate
Guselkumab vs. adalimumab				
Gordon et al., 2015[74] X-PLORE	251	16 weeks	Lower incidence of injection-site reactions with guselkumab (RR, 0.07; 95% CI, 0.01 to 0.33); no significant difference in AEs, SAEs, or withdrawals due to AEs.	Moderate
Blauvelt et al., 2017[69,70] Papp et al., 2018[70] VOYAGE-1	663[a]	16 weeks	No significant differences in AEs, SAEs, withdrawals due to AEs, or injection-site reactions.	Moderate
Reich et al., 2017[73] Reich et al., 2019[71] Gordon et al., 2018[72] VOYAGE-2	744[a]	16 weeks	Lower incidence of injection-site reactions with guselkumab (RR, 0.38; 95% CI, 0.19 to 0.74); no significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Guselkumab vs. secukinumab				
Reich et al., 2019[44] Blauvelt et al., 2021[80] ECLIPSE	1,048	48 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Ixekizumab vs. guselkumab				
Blauvelt et al., 2020[17] Blauvelt et al., 2021[36] IXORA-R	1,027	24 weeks	Higher risk of injection-site reaction for ixekizumab than guselkumab; no significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Ixekizumab vs. secukinumab				
AlMutairi et al., 2020[23]	54	24 weeks	No significant differences in total AEs or injection-site reactions; no serious AE or withdrawals due to AE in either group.	Moderate
Ixekizumab vs. ustekinumab				
Reich et al., 2017[47] Paul et al., 2018[48] Wasel et al., 2020[79] Puig et al., 2020[83,136] IXORA-S	302	24 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Risankizumab vs. adalimumab				
Reich et al., 2019[46] IMMVENT	605	16 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Risankizumab vs. secukinumab				
Warren et al., 2021[19] IMMerge	327	52 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Risankizumab vs. ustekinumab				
Papp, et al., 2017[52]	166	48 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Gordon et al., 2018[67] UlttIMMA-1	506	52 weeks	Significantly fewer SAEs during weeks 0 to 16 with risankizumab vs. ustekinumab, but similar incidence during weeks 17 to 52 and similar incidence of AEs and withdrawals due to AEs.	Moderate
Gordon et al., 2018[67] UltIMMA-2	393	52 weeks	Significantly fewer AEs during weeks 17 to 52 for risankizumab vs. ustekinumab, similar incidence of AEs during weeks 0 to 16 and similar incidence of SAEs and withdrawals due to AEs throughout study.	Moderate
Secukinumab vs. ustekinumab				
Blauvelt et al., 2017[41,42] Thaci et al., 2015[40] CLEAR	676	52 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Bagel et al., 2018[39] Bagel et al., 2021[77] CLARITY	1,102	52 weeks	No significant differences in AEs, SAEs or withdrawals due to AEs. Injection-site reactions were NR.	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Tildrakizumab vs. etanercept				
Reich et al., 2017[65] reSURFACE-2	1,090	28 weeks	No significant difference in SAEs or withdrawals due to AE during entire study period; significantly fewer AEs for 100-mg dose during entire study period; no difference in AEs for 200-mg dose during weeks 0 to12 but significantly lower AEs for 200-mg dose during weeks 13 to 28.	Moderate
Bimekizumab (pipeline drug) vs. adalimumab				
Warren et al., 2021[25] BE SURE	478	24 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Bimekizumab (pipeline drug) vs. placebo				
Papp et al., 2018[38] BE ABLE	250	12 weeks	AEs more common at higher doses of active drug vs. placebo; no significant differences in SAEs or withdrawals due to AEs for any doses. Injection-site reactions were NR.	Moderate
Gordon et al., 2021[22] BE READY	435	16 weeks	Higher risk of AEs for bimekizumab than placebo (61% vs. 41%; RR, 1.5; 95% CI, 1.1 to 2.0). No significant differences in SAEs, and withdrawals due to AEs were rare.	Moderate
Glatt et al., 2017[53]	39	One infusion, 20 weeks follow-up	No significant differences in AEs, SAEs, or withdrawals due to AEs. Injection-site reactions were NR.	Moderate
Reich et al., 2021[21] BE VIVID	567	52 weeks	Other than lower risk of withdrawals due to AEs for bimekizumab vs. placebo, no significant differences between bimekizumab and placebo or ustekinumab.	Moderate
Bimekizumab (pipeline drug) vs. secukinumab				
Reich et al., 2021[24] BE RADIANT	743	48 weeks	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Deucravacitinib (pipeline drug) vs. placebo				
Papp et al., 2018[54]	268	12 weeks	AEs more common at higher doses of active drug vs. placebo; no significant differences in SAEs or withdrawals due to AEs for any doses. Injection-site reactions were NR.	Moderate

Notes: [a] Not including the placebo arm.
Abbreviations. AE: adverse event; CI: confidence interval; NR: not reported; RCT: randomized controlled trial; RR: risk ratio; SAE: serious adverse event; TIM: targeted immune modulator; vs.: versus.

Table 5. Comparisons of TIMs in RCTs for General Tolerability in Plaque Psoriasis

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Apremilast vs. etanercept						
Reich et al., 2017[49] LIBERATE	250 16 weeks	1.3 (1.05 to 1.7)	1.5 (0.26 to 8.7)	1.5 (0.26 to 8.7)	NA (comparing oral to injectable)	Moderate
Brodalumab vs. ustekinumab						
Lebwohl et al., 2015[37] AMAGINE-2	1,831 52 weeks	0.98 (0.87 to 1.1)	1.47 (0.30 to 7.2)	0.74 (0.21 to 2.6)	NR	Moderate
Lebwohl et al., 2015[37] AMAGINE-3	1,881 52 weeks	1.1 (0.93 to 1.2)	2.52 (0.30 to 21.4)	2.26 (0.49 to 10.4)	NR	Moderate
Certolizumab pegol vs. etanercept						
Lebwohl et al., 2018[15] CIMPACT	502 (without the placebo arm) 12 weeks	200 mg: 1.02 (0.81 to 1.3) 400 mg: 1.06 (0.85 to 1.3)	RR (95% CI) 200 mg: 0.25 (0.03 to 2.3) 400 mg: 0.25 (0.03 to 2.2)	RR (95% CI) 200 mg: 1.02 (0.06 to 16.1) 400 mg: 4.0 (0.45 to 35.6)	NR	Moderate
Etanercept vs. infliximab						
De Vries et al., 2017[64] PIECE	48 24 weeks	1.04 (0.93 to 1.2)	0.72 (0.13 to 4.0)	1.09 (0.07 to 16.4)	0.36 (0.08 to 1.6)	High
Etanercept vs. ixekizumab[a]						
Griffiths et al., 2015[68] UNCOVER-2 UNCOVER-3	2,570 12 weeks	0.93 (0.85 to 1.02)	0.75 (0.32 to 1.76)	0.99 (0.48 to 2.07)	1.05 (0.78 to 1.4)	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Etanercept vs. secukinumab						
Langley et al., 2014[45] FIXTURE	1,306 52 weeks	0.97 (0.90 to 1.1)[b]	1.24 (0.58 to 2.6)[b]	1.07 (0.61 to 1.9)[b]	14.90 (6.7 to 33.2)[c]	Moderate
Etanercept vs. tofacitinib[d]						
Bachelez et. al., 2015[62] Valenzuela et al., 2016[63] OPT	1,106 12 weeks	5 mg: 1.1 (0.92 to 1.2) 10 mg: 0.96 (0.84 to 1.1)	5 mg: 3.6 (1.01 to 12.8) 10 mg: 1.1 (0.47 to 2.5)	5 mg: 0.98 (0.35 to 2.8) 10 mg: 1.1 (0.39 to 3.4)	NA (comparing oral to injectable)	Moderate
Etanercept vs. ustekinumab[e]						
Griffiths, et al. 2010,[51]	903 12 weeks	1.03 (0.94 to 1.13)	1.60 (0.61 to 4.23)	0.80 (0.24 to 2.64)	6.26 (4.00 to 9.81)[f]	Moderate
Guselkumab vs. adalimumab						
Gordon et al., 2015[74] X-PLORE	251 16 weeks	0.89 (0.66 to 1.20)	0.35 (0.09 to 1.39)	0.62 (0.07 to 5.85)	0.07 (0.01 to 0.33)	Moderate
Blauvelt et al., 2017[69,70] Papp et al., 2018[70] VOYAGE-1	663 16 weeks	1.01 (0.87 to 1.17)	1.35 (0.30 to 6.0)	1.35 (0.47 to 3.9)	0.40 (0.16 to 1.03)	Moderate
Reich et al., 2017[73] Reich et al., 2019[71] Gordon et al., 2018[72] VOYAGE-2	744 16 weeks	0.98 (0.84 to 1.2)	0.88 (0.26 to 3.0)	0.67 (0.25 to 1.9)	0.38 (0.19 to 0.74)	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Guselkumab vs. secukinumab						
Reich et al., 2019[44] ECLIPSE	1,048 48 weeks	0.95 (0.90 to 1.02)	0.80 (0.35 to 1.8)	0.85 (0.54 to 1.3)	NR	Moderate
Ixekizumab vs. guselkumab						
Blauvelt et al., 2020[17] Blauvelt, et al., 2021[36] IXORA-R	1,027 24 weeks	1.1 (0.99 to 1.2)	1.8 (0.8 to 4.3)	1.1 (0.6 to 2.1)	3.4 (2.1 to 5.6)	Moderate
Ixekizumab vs. secukinumab						
AlMutairi et al., 2020[23]	54 24 weeks	1.04 (0.71 to 1.5)	None	None	1.2 (0.35 to 3.9)	Moderate
Ixekizumab vs. ustekinumab						
Reich et al., 2017[47] Paul et al., 2018[48] IXORA-S	302 24 weeks	0.92 (0.80 to 1.07)	2.46 (0.23 to 26.83)	0.74 (0.18 to 3.03)	NR	Moderate
Risankizumab vs. adalimumab						
Reich et al., 2019[46] IMMVENT	605 16 weeks	0.98 (0.85 to 1.1)	0.67 (0.19 to 2.4)	1.1 (0.46 to 2.7)	NR	Moderate
Risankizumab vs. secukinumab						
Warren et al., 2021[19] IMMerge	327 52 weeks	1.002 (0.87 to 1.2)	0.25 (0.05 to 1.2)	1.5 (0.54 to 4.1)	NR	Moderate
Risankizumab vs. ustekinumab						
Papp, et al., 2017[52]	166 48 weeks	1.11 (0.87 to 1.42)	0.98 (0.06 to 15.07)	1.95 (0.52 to 7.27)	NR	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Gordon et al., 2018[67] UlttIMMA-1	506 52 weeks	Weeks 0 to 16: 0.99 (0.79 to 1.25) Weeks 17 to 52: 0.92 (0.78 to 1.09)	Weeks 0 to 16: 0.33 (0.05 to 2.31) Weeks 17 to 52: 0.33 (0.0 to 84.9)	Weeks 0 to 16: 0.29 (0.11 to 0.77) Weeks 17 to 52: 1.33 (0.46 to 3.9)	NR	Moderate
Gordon et al., 2018[67] UltIMMA-2	393 52 weeks	Weeks 0 to 16: 0.85 (0.68 to 1.1) Weeks 17 to 52: 0.75 (0.64 to 0.87)	Weeks 0 to 16: 1.4 (0.02 to 107.4) Weeks 17 to 52: 0.32 (0.05 to 2.3)	Weeks 0 to 16: 0.67 (0.17 to 2.64) Weeks 17 to 52: 1.05 (0.35 to 3.2)	NR	Moderate
Secukinumab vs. ustekinumab						
Blauvelt et al., 2017[41,42] Thaci et al., 2015[40] CLEAR	676 52 weeks	1.1 (0.98 to 1.24) at 16 weeks 1.0 (0.97 to 1.1) at 52 weeks	0.75 (0.17 to 3.34) at 16 weeks 1.1 (0.46 to 2.7) at 52 weeks	1.0 (0.42 to 2.38) at 16 weeks 1.1 (0.68 to 1.8) at 52 weeks	NR	Moderate
Bagel et al., 2018[39,77] CLARITY	1,102 52 weeks	1.0 (0.90 to 1.2) at 16 weeks 0.97 (0.90 to 1.05) at 52 weeks	1.6 (0.62 to 4.0) at 16 weeks 1.62 (0.82 to 3.21) at 52 weeks	1.6 (0.68 to 3.6) at 16 weeks 1.4 (0.80 to 2.4) at 52 weeks	NR	Moderate
Tildrakizumab vs. etanercept						
Reich et al., 2017[65] RESURFACE 2	1,090 28 weeks	*Weeks 0 to 12* Tildrakizumab 100 mg: 0.82 (0.70 to 0.96) Tildrakizumab 200 mg: 0.91 (0.79 to 1.06) *Weeks 13 to 28* Tildrakizumab 100 mg: 0.81 (0.69 to 0.95) Tildrakizumab 200 mg: 0.80 (0.68 to 0.93)	*Weeks 0 to 12* Tildrakizumab 100 mg: 0.51 (0.13 to 2.02) Tildrakizumab 200 mg: 0.50 (0.13 to 1.98) *Weeks 13 to 28* Tildrakizumab 100 mg: 0.33 (0.03 to 3.13) Tildrakizumab 200 mg: 0.32 (0.03 to 3.08)	*Weeks 0 to 12* Tildrakizumab 100 mg: 0.58 (0.17 to 1.97) Tildrakizumab 200 mg: 0.85 (0.29 to 2.51) *Weeks 13 to 28* Tildrakizumab 100 mg: 0.63 (0.28 to 1.44) Tildrakizumab 200 mg: 0.41 (0.16 to 1.06)	*Weeks 0 to 12* Tildrakizumab 100 mg: 0.08 (0.02 to 0.31) Tildrakizumab 200 mg: 0.07 (0.02 to 0.31) *Weeks 13 to 28* Tildrakizumab 100 mg: 0.98 (0.20 to 4.83) Tildrakizumab 200 mg: 0.32 (0.03 to 3.08)	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Bimekizumab (pipeline drug) vs. adalimumab						
Warren et al., 2021[25] BE SURE	478 24 weeks	Bimekizumab every 4 weeks: 1.01 (0.88 to 1.2), *P* = .84 Bimekizumab every 4 weeks then every 8 weeks: 1.03 (0.90 to 1.2), *P* = .66	Bimekizumab every 4 weeks: 0.60 (0.15 to 2.5), *P* = .51 Bimekizumab every 4 weeks then every 8 weeks: 1.2 (0.37 to 3.8), *P* = .79	Bimekizumab every 4 weeks: 0.81 (0.22 to 2.9), *P* = 0.76 Bimekizumab every 4 weeks then every 8 weeks: 0.20 (0.02 to 1.7), *P* = .12	NR	Moderate
Bimekizumab (pipeline drug) vs. placebo						
Papp et al., 2018[38] BE ABLE	250 12 weeks	1.7 (1.1 to 2.6)	2.0 (0.27 to 15.4)	0.20 (0.01 to 3.2)	NR	Moderate
Gordon et al., 2021[22] BE READY	435 16 weeks	1.5 (1.1 to 2.0)	Not able to calculate, zero events in 1 group	0.74 (0.15 to 3.6)	NR	Moderate
Glatt et al., 2017[53]	39 1 infusion, 20 weeks of follow-up	1.1 (0.78 to 1.5)	1.0 (0.004 to 249)	2.0 (0.03 to 155.1)	NR	Moderate
Reich et al., 2021 [21] BE VIVID	567 52 weeks	Bimekizumab vs. placebo: 1.2 (0.94 to 1.5) Bimekizumab vs. ustekinumab: 1.1 (0.93 to 1.3)	Bimekizumab vs. placebo: 0.26 (0.09 to 0.78) Bimekizumab vs. ustekinumab: 1.0 (0.26 to 4.0)	Bimekizumab vs. placebo: 0.65 (0.13 to 3.3) Bimekizumab vs. ustekinumab: 0.51 (0.15 to 1.7)	NR	Moderate
Bimekizumab (pipeline drug) vs. secukinumab						
Reich et al., 2021[24] BE RADIANT	743 48 weeks	1.06 (0.99 to 1.1)	1.3 (0.57 to 2.9)	1.04 (0.58 to 1.9)	NR	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawal Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/Infusion Reactions: RR (95% CI)	Risk of Bias
Deucravacitinib (pipeline drug) vs. placebo						
Papp et al., 2018[54]	268 12 weeks	Compared with placebo 3 mg every other day: 1.16 (0.79 to 1.7) 3 mg daily: 1.07 (0.72 to 1.6) 3 mg twice daily: 1.26 (0.88 to 1.8) 6 mg twice daily: 1.57 (1.1 to 2.2) 12 mg daily: 1.51 (1.09 to 2.10)	Compared with placebo 3 mg every other day: 0.51 (0.05 to 5.44) 3 mg daily: 1.02 (0.15 to 6.9) 3 mg twice daily: 0.50 (0.05 to 5.3) 6 mg twice daily: 1.50 (0.26 to 8.6) 12 mg daily: 0.51 (0.05 to 5.4)	Compared with placebo 3 mg every other day: 1.02 (0.70 to 15.84) 3 mg daily: 1.02 (0.70 to 15.84) 3 mg twice daily: 1 (0.065 to 15.5) 6 mg twice daily: 1.0 (.0.004 to 252) 12 mg daily: 1.0 (0.004 to 257)	NA (oral agent)	Moderate

Notes: All entries in this table are calculated values from the data provided in the articles. [a] Study authors reported pooled results from UNCOVER 2 and UNCOVER 3 for harms; the RRs calculated and reported in this table are for the every-2-week dosage of ixekizumab. [b] RR calculated for the FDA-approved dose (300 mg) of secukinumab. [c] RR calculated for pooled data from 150-mg and 300-mg doses of secukinumab. [d] Doses are administered twice daily. The 5-mg twice daily dosage is the FDA-approved dosage. [e] Data are for the combined 45-mg and 90-mg dosages of ustekinumab. [f] Participants in the etanercept received more injections than those in the ustekinumab group.
Abbreviations. AE: adverse event; CI: confidence interval; FDA: US Food and Drug Administration; NA: not applicable; NR: not reported; RCT: randomized controlled trial; RR: risk ratio; SAE: serious adverse event; TIM: targeted immune modulator; vs.: versus.

Harms Reported in Cohort Studies

Table 6 summarizes harm outcomes from 10 cohort studies.[27-32,57-59,85,88,126] Six of these studies were new to this update.[27-32] All studies evaluated individuals with plaque psoriasis; 4 studies also included persons with psoriatic arthritis.[27,30,31,58] We evaluated 1 study[29] as high RoB; the rest we evaluated as moderate RoB. Appendix B, Table B3 provides detailed study characteristics and findings.

Five cohort studies were conducted with participants identified through US insurance claims for biologic therapy with diagnosis codes for psoriasis (and psoriatic arthritis as well, in some studies).[27,30,57-59] The number of participants evaluated in these studies ranged from 9,305 to 123,383, and many of these studies used the same databases (MarketScan, Optum Labs) to identify participants, but covered different but overlapping time periods. Thus, they cannot be considered truly independent cohorts. The specific biologic agents evaluated, the comparators against which agents were evaluated, and the harm outcomes reported varied across studies. With respect to infection outcomes, Dommasch and colleagues reported a significantly lower risk of serious infection with apremilast or etanercept, a significantly higher risk for infliximab, and no difference for ustekinumab as compared with adalimumab (Table 6).[59] Wu and colleagues reported no significant differences in the risk of adverse medical conditions for etanercept, ustekinumab, or infliximab when compared with adalimumab.[57] Jin and colleagues reported a significantly lower incidence of hospitalization for serious infection for ustekinumab compared with adalimumab, apremilast, etanercept, golimumab, infliximab, ixekizumab, and secukinumab (adjusted hazard ratio [HR] range, 1.39 to 2.98), with no difference compared with certolizumab pegol.[27] Li and colleagues reported somewhat similar findings as Jin and colleagues; fewer serious infections with IL-12/23 agents (ustekinumab) compared with anti-TNF-α agents (HR 0.59; 95% CI, 0.39 to 0.90) but similar incidence between anti-IL-17 agents and anti-TNF-α agents and similar incidence between anti-IL-17 and anti-IL 12/23 agents.[30] Lee and colleagues reported no significant differences in incident atrial fibrillation or major cardiovascular event between ustekinumab and anti-TNF-α agents.[58]

Three studies were conducted with participants identified from prospective registries of individuals with psoriasis.[29,32,55] The British Association of Dermatologists Biologic Interventions Register (BADBIR) is a prospective registry of patients from 157 dermatology centers in the UK and Republic of Ireland supported by multiple drug manufacturers for pharmacovigilance activities.[32,55] Using participants identified through BADBIR, Warren and colleagues reported a statistically significant higher risk for drug discontinuation for AEs with infliximab compared with adalimumab (RR, 2.82; 95% CI, 1.79 to 4.45) and a statistically significant lower risk for ustekinumab compared with adalimumab (RR, 0.60; 95% CI, 0.39 to 0.92).[55] No significant differences in withdrawals due to AEs were observed comparing adalimumab to etanercept.[55] Rungapiromnan and colleagues also identified participants from BADBIR and reported no significant differences in major cardiovascular events among users of adalimumab, etanercept or ustekinumab.[32] Munera-Campos and colleagues identified participants from the prospective BIOBADADERM registry that covers 18 hospitals in Spain and includes individuals with psoriasis who take biologic agents.[29] Study authors focused their analysis specifically on hepatic AEs.[29] Study authors observed no hepatic AEs for users of apremilast.[29] Compared with anti-TNF-α agents, they observed a higher incidence of nonalcoholic fatty liver disease for users of anti-IL-17

agents (adjusted incidence rate ratio [IRR], 4.16; 95% CI, 1.36 to 12.70) and no difference for users of anti-IL-23 agents.[29] Authors observed no significant differences in liver test abnormalities or overall hepatic AEs for anti-IL-17 or anti-IL 23 agents compared with anti-TNF-α agents.[29]

Two cohort studies identified participants through national health databases.[28,31] Penso and colleagues used national health databases in France to identify individuals with psoriasis who were new users of biologic agents.[28] Compared with etanercept, risk for serious infection was significantly increased with adalimumab (adjusted HR, 1.22; 95% CI, 1.07 to 1.38) and infliximab (adjusted HR, 1.79; 95% CI, 1.49 to 2.16) and significantly decreased for ustekinumab (adjusted HR, 0.79; 95% CI, 0.67 to 0.94).[28] Authors observed no significant differences between etanercept and the other agents evaluated (apremilast, brodalumab, certolizumab pegol, guselkumab, ixekizumab, and secukinumab).[28] However, this study also reported additional head-to-head comparisons; we summarize them in Table 6, and report them in detail in Appendix B, Table B3. In brief, statistically significant comparisons were observed on the outcome of serious infections for the following head-to-head comparisons: apremilast (lower incidence) versus adalimumab, apremilast (lower incidence) versus infliximab, certolizumab pegol (lower incidence) versus infliximab, certolizumab pegol versus ustekinumab (lower incidence), infliximab versus adalimumab (lower incidence), infliximab versus ustekinumab (lower incidence), ixekizumab (lower incidence) versus infliximab, and ustekinumab (lower incidence) versus adalimumab.

Srinivas and colleagues used multiple national registers and health databases in Sweden to identify individuals with psoriasis and psoriatic arthritis who were new users of secukinumab or ustekinumab.[31] Authors reported a statistically significantly increased use of antibiotics for respiratory infection and urinary infection for secukinumab compared with ustekinumab (adjusted IRR, 1.22; 95% CI, 1.03 to 1.43), but no significant differences in serious respiratory or urinary infection or candidiasis.[31]

Table 6. Summary of Observational Studies for Harms in Adults Receiving TIMs for Plaque Psoriasis

Authors, Year	Number of Participants	Follow-up	Comparisons[a]	Population	Results	Risk of Bias
Dommasch et al., 2019[59]	107,707	NR	New users of methotrexate, adalimumab, acitretin, apremilast, etanercept, infliximab, ustekinumab	Adults with psoriasis with at least 3 ICD-9-CM codes of 696.1 on separate dates identified through insurance claims 2003 to 2017	Compared with adalimumab, HR; 95% CI) of serious infection requiring hospitalization: • Apremilast: 0.31; 0.15 to 0.65 • Etanercept: 0.76; 0.61 to 0.94 • Infliximab: 1.9; 1.01 to 3.60 • Ustekinumab: 0.70; 0.49 to 1.00	Moderate
Jin et al., 2021[27]	123,383	117,744 person-years	Ustekinumab, adalimumab, apremilast, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, secukinumab; doses as prescribed in usual care	Adults with plaque psoriasis or psoriatic arthritis identified as new initiators of 1 of 9 biologics or small molecules in health claim databases	Ustekinumab had lower hospitalization for serious infection vs. adalimumab, apremilast, etanercept, infliximab, ixekizumab, and secukinumab. No significant difference vs. certolizumab pegol or golimumab.	Moderate
Lee et al., 2019[58]	60,028	Mean (SD) 1.4 (1.3) years, max 6.0 years	Ustekinumab TNF-α inhibitors	Adults with psoriasis or psoriatic arthritis who initiated therapy with ustekinumab or a TNF-α inhibitor identified through US insurance claims between 2009 and 2015	No significant difference for incident atrial fibrillation or major cardiovascular events comparing ustekinumab with anti-TNF-α inhibitors	Moderate

Authors, Year	Number of Participants	Follow-up	Comparisons[a]	Population	Results	Risk of Bias
Li et al., 2020[30]	11,560 treatment episodes (9,305 persons)	Median 0.6 years (IQR, 0.2 to 1.1) per episode	Anti-IL-17 (ixekizumab, secukinumab) vs. anti-IL-12/23 (ustekinumab) vs. TNF-α (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab)	Adults with diagnosis code for psoriasis or psoriatic arthritis with pharmacy or infusion claim for biologics of interest	Significantly fewer serious infections with IL-12/23 (ustekinumab) vs. anti-TNF-α drugs (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab); similar rates between IL-17 (ixekizumab or secukinumab) and anti-TNF-α and between IL-17 and IL-12/23	Moderate
Munera-Campos et al., 2021[29]	3,171	11,200 patient-years	Anti-IL 23 vs. anti-IL 17 vs. apremilast vs. anti-TNF-α	Persons with psoriasis receiving biologic therapy identified through a multicenter, prospective registry	Higher incidence of nonalcoholic fatty liver disease for anti-IL17 agents vs. anti-TNF-α agents, no difference for anti-IL 23 agents. Compared with anti-TNF-α agents, no differences in liver test abnormalities or in total hepatic AEs for anti-IL 17 or anti-IL 23 agents. No hepatic AEs for apremilast.	High
Penso et al., 2021[28]	44,239	Median 12 (IQR, 7 to 24) months	Adalimumab vs. apremilast vs. brodalumab vs. certiolizumab pegol vs. guselkumab vs. etanercept vs. infliximab vs. ixekizumab vs. secukinumab vs. ustekinumab	Adults with psoriasis identified through national data systems who were new users of biologic treatments	Compared with etanercept, time to first serious infection significantly greater with adalimumab and infliximab and significantly lower with ustekinumab. No significant differences between other agents evaluated and etanercept. Multiple other head-to-head comparisons reported (see Appendix B, Table B3).	Moderate

Authors, Year	Number of Participants	Follow-up	Comparisons[a]	Population	Results	Risk of Bias
Rungapiromnan et al., 2020[32]	5,468	Median follow-up: 1.7 to 1.8 years	Ustekinumab vs. etanercept or adalimumab	Adults with moderate-to-severe psoriasis treated with biologic therapies between 2007 and 2016	No significant differences in major cardiovascular events between ustekinumab, adalimumab, and etanercept	Moderate
Srinivas et al., 2020[31]	1,955	Between 2 and 8 years	Secukinumab vs. ustekinumab	Adults with psoriasis and psoriatic arthritis who were new users of secukinumab or ustekinumab identified through national registers	Statistically significant increased use of antibiotics for respiratory and urinary infections for secukinumab vs. ustekinumab, but no difference in serious respiratory or urinary infections, and no difference in candidiasis	Moderate
Warren et al., 2015[55]	3,523	Varied	Adalimumab vs. etanercept vs. infliximab vs. ustekinumab	Biologically naïve adults with psoriasis identified from a prospective dermatological pharmacovigilance patient registry 2007 to 2014	Discontinuation due to AEs • Infliximab vs. adalimumab RR, 2.8; 95% CI, 1.8 to 4.5 • Ustekinumab vs. adalimumab • RR, 0.60; 95% CI, 0.39 to 0.92 • Etanercept vs. adalimumab • RR 0.77; 95% CI, 0.58 to 1.02	Moderate
Wu et al., 2018[57]	10,065	8.3 to 11.9 months	Adalimumab vs. etanercept, ustekinumab, or infliximab	Adults who were biologic-naïve with > 2 psoriasis diagnoses on insurance claims during the study period. Analyses restricted to participants treated with monotherapy	No statistically significant differences in the risk of adverse medical conditions between participants treated with adalimumab vs. those treated with other biologic therapies (etanercept, ustekinumab, and infliximab)	Moderate

Notes. [a] Doses not reported for nearly all studies.
Abbreviations. AE: adverse event; CI: confidence interval; HR: hazard ratio; ICD-9-CM: International Classification of Disease, 9th edition, clinical modification; IL: interleukin; IQR: interquartile range; NR: not reported; RR: risk ratio; SD: standard deviation; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha; vs.: versus.

Efficacy and Harms of Pipeline TIM Agents for Plaque Psoriasis

We identified 7 RCTs[21,22,24,25,38,53,54] reporting on the efficacy and harms of 2 pipeline TIM agents: bimekizumab and deucravacitinib. Four are new to this update.[21,22,24,25] Table 7 shows the Summary of Findings (GRADE) for these pipeline agents. Tables 3, 4, and 5 provide a summary of this evidence. Appendix B, Tables B1 and B2 provide detailed study characteristics and results, and Appendix D describes efficacy outcome measures used in included RCTs. We rated all studies as moderate RoB because of extensive manufacturer involvement in study design, execution, and reporting.

Table 7. Summary of Findings (GRADE) of Pipeline TIMs for Plaque Psoriasis

Outcome	Certainty of Evidence	Relationship[a]
Bimekizumab vs. placebo[b]		
Disease remission (4 RCTs)	●●●● (high)	Favors bimekizumab
QoL (2 RCTs)	●●●○ (moderate)	Favors bimekizumab
AEs (2 RCTs)	●●○○ (low)	Favors placebo
SAEs (2 RCTs)	●●○○ (low)	No difference
Bimekizumab vs. adalimumab[c]		
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 vs. secukinumab[c]		
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 vs. ustekinumab[c]		
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
Deucravacitinib vs. placebo		
Clinical improvement (1 RCT)	●●●○ (moderate)	Favors deucravacitinib
QoL (1 RCT)	●●●○ (moderate)	Favors deucravacitinib
AEs (1 RCT)	●●○○ (low)	Favors placebo
SAEs (1 RCT)	●●○○ (low)	Uncertain

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] New studies for previously included comparison for this update. [c] New comparison for this update.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluation approach; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event; TIM: targeted immune modulator.

Bimekizumab vs. Adalimumab

We identified 1 new, moderate-RoB RCT (BE SURE) for this update.[25]

For this multisite, multicountry RCT, authors randomized adults with moderate-to-severe plaque psoriasis to either bimekizumab 320 mg every 4 weeks, bimekizumab 320 mg every 4 weeks for 16 weeks and then every 8 weeks, or adalimumab 40 mg every 2 weeks.[25] At 24 weeks, participants assigned to adalimumab were switched to bimekizumab 4 weeks for the duration of the study.[25] The primary study endpoints were PASI 90 and IGA 0 or 1 response at 16 weeks.[25] Secondary outcomes included PASI 100 response at week 16 and week 24 and PASI 90, IGA 0 or 1, and DLQI 0 or 1 at week 24.[25]

Authors combined the 2 bimekizumab dosing intervals for the primary study endpoints.[25] Significantly more participants assigned to bimekizumab (86.2%) achieved a PASI 90 response at week 16 compared with adalimumab (47.2%; calculated RR, 1.8; 95% CI, 1.5 to 2.2).[25] Authors observed similar findings for the IGA 0 or 1 and PASI 100 responses at week 16 and for all outcomes reported at week 24. Both dosing intervals of bimekizumab evaluated were more effective than adalimumab on the outcomes reported at week 24.[25]

Bimekizumab vs. Secukinumab

We identified 1 new, moderate-RoB RCT (BE RADIANT) for this update.[24]

Adults with moderate-to-severe plaque psoriasis for at least 6 months in this multisite, multicountry study were randomized to bimekizumab 320 mg every 4 weeks until week 16 or to secukinumab 300 mg weekly to week 4 then every 4 weeks.[24] At week 16, participants receiving bimekizumab were rerandomized to either continue every 4 weeks or to change to every 8 weeks for maintenance.[24] The primary study endpoint was a PASI 100 response at 16 weeks' follow-up; secondary outcomes included additional PASI response measures, IGA 0 or 1, and DLQI 0 or 1 at either 16 or 48 weeks.[24]

A higher proportion of participants assigned to bimekizumab (61.7%) reported a PASI 100 response at 16 weeks compared with secukinumab (48.9%; ARD, 12.7%; 95% CI, 5.8 to 19.6).[24] Authors observed a similar pattern for most other secondary endpoints at 16 weeks (PASI 90, IGA 0 or 1); however, there was no significant difference for the PASI 75 response (calculated RR, 1.02; 95% CI, 0.98 to 1.1).[24] The 2 dosing regimens of bimekizumab combined remained more effective than secukinumab at 48 weeks of follow-up, we calculated the RR for the PASI 100 response as 1.5 (95% CI, 1.3 to 1.7), and significantly larger responses were also observed for the PASI 90, PASI 75, IGA 0 or 1, and DLQI 0 or 1.[24] When authors evaluated the 2 separate bimekizumab dosing intervals separately compared with secukinumab, both doses were significantly more effective than secukinumab.[24]

Bimekizumab vs. Ustekinumab

We identified 1 new, moderate-RoB RCT (BE VIVID) for this update.[21]

In this multisite, multicountry RCT, adults with moderate-to-severe plaque psoriasis for at least 6 months were randomized to bimekizumab 320 mg every 4 weeks or ustekinumab (45 mg or 90 mg depending on weight) at weeks 0 and 4 then every 12 weeks.[21] This study also included a placebo group for the first 16 weeks; at week 16, placebo group participants were switched to

bimekizumab 320 mg every 4 weeks for the duration of the study.[21] The primary study endpoints were PASI 90 and IGA 0 or 1 responses at week 16.[21] Secondary outcomes included PASI 100, PASI 75, IGA 0, DLQI 0 or 1, and various itch, scaling, scalp, and pain measures at weeks 16 and 52.[21]

At week 16, a significantly higher proportion of participants assigned to bimekizumab (85%) achieved a PASI 90 response compared with participants assigned to ustekinumab (50%, calculated RR, 1.7; 95% CI, 1.5 to 2.0).[21] Authors observed similar findings for IGA 0 or 1, PASI 100, IGA 0, DLQI 0 or 1, Psoriasis Symptoms and Impacts Measure (P-SIM) itch and scaling scores, and scalp IGA response, but no differences on P-SIM pain score.[21] Bimekizumab remained more effective than ustekinumab for all week 52 outcomes reported.[21]

Bimekizumab vs. Placebo

We identified 2 new RCTs[21,22] in addition to the 2 RCTs included in the previous review.[38,53]

All were moderate RoB and compared various doses of bimekizumab with placebo among persons with moderate-to-severe plaque psoriasis.[38,53] Glatt and colleagues was a phase 1, first-in-human trial that administered various doses between 8 mg and 640 mg as a single infusion and reported outcomes over 20 weeks with AEs designated as the primary study endpoints.[53] BE ABLE was a phase 2b trial that evaluated various doses administered every 4 weeks and reported outcomes at 12 weeks.[38] BE READY[22] was a phase 3 trial that evaluated a 320-mg dose every 4 weeks for 16 weeks compared with placebo, and BE VIVID,[21] also a phase 3 trial, evaluated a 320-mg dosage compared with placebo and also compared with an active comparator (ustekinumab). BE ABLE,[38] BE READY,[22] and BE VIVID[21] all reported a PASI 90 response as the primary study endpoint.

Although safety was the primary study endpoint in the Glatt and colleagues study, clinical efficacy was evaluated and statistically significant differences between placebo and all doses evaluated were observed at all time points for the lesion severity score, and for the higher dosages evaluated (160 mg, 480 mg, 640 mg) at nearly all time points for percent change from baseline for PASI and PGA.[53] In BE ABLE, the proportion of participants achieving PASI 90 response varied from 46% to 79% across all bimekizumab doses and was 0% in the placebo group ($P < .001$ for all dose comparisons to placebo).[38] Similar findings were observed on all secondary remission and clinical improvement outcomes.[38] In BE READY, a statistically significant higher proportion achieved a PASI 90 response at 16 weeks for bimekizumab (93%) compared with placebo (1%; calculated RR, 78.1; 95% CI, 11.1 to 548.3).[22] Authors observed similar responses for the PASI 100, the IGA 0 or 1, DLQI 0 or 1, and other secondary outcomes.[22] In BE VIVID, significantly more participants assigned to bimekizumab (85%) achieved a PASI 90 response compared with placebo (5%, calculated RR, 17.7, 95% CI, 6.8 to 46.0).[21] Bimekizumab was also more effective than placebo for all secondary endpoints reported.[21]

With respect to harms, Glatt and colleagues reported no significant differences in AEs compared with placebo (all dosages were pooled).[53] Only 1 SAE occurred overall (in the bimekizumab group).[53] No withdrawals due to AE were observed in either the bimekizumab or placebo group.[53] In the BE ABLE trial, a significant increased risk of AEs was observed for all bimekizumab doses pooled compared with placebo (RR, 1.7; 95% CI, 1.1 to 2.6).[38] Authors

observed no differences in SAEs or withdrawals due to AEs.[38] These findings were replicated in the BE READY trial.[22] In BE READY, authors observed a significantly higher proportion of individuals with AEs with bimekizumab (61%) compared with placebo (41%; calculated RR, 1.5; 95% CI, 1.1 to 2.0), but the risk of SAEs and discontinuations due to AEs were similar between groups.[22] In BE VIVID, no significant difference in AEs was observed (calculated RR, 1.2; 95% CI, 0.94 to 1.50) or in SAEs, and fewer discontinuations occurred with bimekizumab compared with placebo (calculated RR, 0.26; 95% CI, 0.09 to 0.78).[21]

Deucravacitinib vs. Placebo

No new studies were identified for this update.

One moderate-RoB RCT was included in the prior report which evaluated various dosages compared with placebo over 12 weeks among adults who had had moderate-to-severe plaque psoriasis for at least 6 months.[54] Except for the lowest dosage (3 mg every other day), all dosages were more effective than placebo on the primary study endpoint (PASI 75: ARD range, 36 to 72 percentage points) and nearly all secondary remission, clinical improvement, and QoL outcomes.[54]

With respect to harms, overall AEs were more frequent at the higher dosages of the pipeline agent (RR, 1.6; 95% CI, 1.1 to 2.2, for 6 mg twice daily; RR, 1.5; 95% CI, 1.1 to 2.1, for 12 mg daily) compared with placebo.[54] The incidence of SAEs and withdrawals due to AEs was not different between groups.[54]

Psoriatic Arthritis

We identified 8 RCTs[16,18,20,26,33-35,43,50,60,61,66] and 1 cohort study[56] evaluating the effectiveness, comparative effectiveness, or harms of TIMs. Of these studies, 4 are new to this update.[16,18,20,26,33-35] One of these focused on the pipeline drug bimekizumab.[20] Table 8 shows the Summary of Findings (GRADE) for the head-to-head TIM agent comparisons; Appendix C, Table C2 provides detailed evidence profiles.

Table 8. Summary of Findings (GRADE) of TIMs for Psoriatic Arthritis (Comparative Effectiveness and Harms)

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]
Incidence of tuberculosis (1 cohort)	●○○○ (very low)	Favors adalimumab vs. infliximab, no difference vs. etanercept
Adalimumab vs. tofacitinib		
Clinical improvement (1 RCT)	●●○○ (low)	Favors tofacitinib
Disease remission (1 RCT)	●●○○ (low)	Favors tofacitinib[c]
QoL (1 RCT)	●●○○ (low)	Favors adalimumab

Outcome	Certainty of Evidence	Relationship[a]
AEs (1 RCT)	●●○○ (low)	No difference
SAEs (1 RCT)	●○○○ (very low)	No difference
Ixekizumab vs. adalimumab[d]		
Clinical improvement—arthritis (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
Secukinumab vs. adalimumab		
Clinical improvement—arthritis (1 RCT)	●●●○ (moderate)	No difference
Clinical improvement—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 (higher dose only)
AEs (1 RCT)	●●●○ (moderate)	Favors adalimumab
SAEs (1 RCT)	●●○○ (low)	No difference
Ustekinumab vs. TNF-α inhibitors[e]		
Enthesitis remission (1 RCT)	●○○○ (very low)	Favors ustekinumab
Arthritis remission (1 RCT)	●○○○ (very low)	No difference
Skin remission (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 vs. the comparator; for harm outcomes, "favors" refers to a lower incidence of harm relative to the comparator; [b] Adalimumab favored vs. either etanercept of infliximab, infliximab favored vs. 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] Among participants with active enthesitis; [f] As measured by SF-36 PCS but no difference as measured by SF-36 MCS.

Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluation approach; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event; SF-36 MCS: 36-item Short Form Health Survey Mental Health Component Score; SF-36 PCS: 36-item Short Form Health Survey Physical Health Component Score; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha.

Comparative Effectiveness (KQ1)

Seven RCTs[16,18,26,33-35,43,50,60,61,66] reported comparative efficacy outcomes for 6 different head-to-head TIM comparisons. Of these, 3 RCTs are new to this update; 2 of them report on 2 new comparisons for this update,[16,26,35] and 1 of them is a new RCT reporting on a previously included comparison.[18,33,34] All studies enrolled participants with active psoriatic arthritis. We rated 1 RCT as high RoB because of inadequate reporting of methods, differences in baseline characteristics between groups, and lack of adequate statistical analysis.[50] We rated another RCT high RoB because of inadequate reporting of randomization method and allocation concealment, unstandardized agents and doses in the comparison group, and lack of blinding.[43] We rated the remaining RCTs moderate RoB for extensive manufacturer involvement. In this section we describe efficacy findings organized by drug comparisons. Table 9 provides a brief summary of this evidence base and findings. Appendix B, Tables B1 and B2 provide detailed study characteristics and results, and Appendix D describes outcome measures used in included RCTs.

Adalimumab vs. Etanercept and Infliximab

We did not identify any new RCTs for this update.

The previous review included 1 high-RoB, head-to-head randomized trial comparing adalimumab with etanercept and infliximab.[50] In this 12-month trial, 100 participants were randomized to receive 40 mg adalimumab every other week, 25 mg etanercept twice per week, or 5 mg/kg infliximab every 6-to-8 weeks.[50] An induction regimen for infliximab was not described and the source of study sponsorship was not disclosed.[50] Dose adjustment was permitted for infliximab in this trial.[50] Participants who had previously trialed anti-TNF-α drugs were excluded, as were participants taking more than 10 mg prednisolone daily or requiring increasing amounts of NSAIDs.[50] The FDA-approved dose for etanercept is 50 mg twice weekly.[131]

The RoB of this trial[50] was difficult to assess because of poor reporting. Neither the method of randomization nor the method of allocation concealment is described. The authors do not declare which outcomes are primary or secondary, nor do they conduct any statistical adjustment for the baseline differences in the groups (the infliximab group had less severe joint disease at baseline, and the etanercept group had more severe skin disease).

The outcomes assessed in this trial were not designated as “primary” or “secondary” but included: ACR20 response, PASI, HAQ, tender joint count, and swollen joint count.[50] Efficacy results indicated that the 3 groups experienced no difference in improvements. The proportion of participants achieving an ACR20 response at 12 months was: adalimumab 70%; etanercept 72%; infliximab 75% (*P* value NR).[50] The authors reported on other outcomes, but they did not say whether adjustment for multiple testing was performed, and they did not adjust for differences in baseline characteristics of the groups, so these results are not reliable. The authors observed no statistically significant differences in the median number of tender joints ($P = .12$), swollen joints ($P = .23$), or HAQ ($P = .60$).[50] Significant differences in median PASI at 1 year were observed (etanercept 2, adalimumab 0.1, infliximab 0; $P < .01$).[50]

Adalimumab vs. Tofacitinib

We did not identify any new RCTs for this update.

The previous review included 1 multicenter, phase 3 RCT (OPAL Broaden) that compared adalimumab with 2 regimens of tofacitinib (5 mg twice daily and 10 mg twice daily) or placebo.[60,61] Participants had not previously tried TNF-α inhibitors but had experienced treatment failure with a DMARD. More than 75% of participants used concomitant methotrexate.[60,61] The manufacturer of tofacitinib funded the study, and we rated it as moderate RoB because of extensive manufacturer involvement in the study design, execution, and reporting. The FDA-approved dose of tofacitinib is 5 mg twice daily.[134]

This trial was designed to evaluate superiority of tofacitinib compared with placebo; it was not designed to show superiority or noninferiority between the active drug groups and no statistical testing was conducted among active treatment groups. The ACR20 response at 12 months was 60% in the adalimumab group versus 70% in the tofacitinib 10 mg group and 68% in the tofacitinib 5 mg group.[60] The ACR50 and ACR70 and PASI 75 responses at 12 months followed a similar pattern.[60] Post hoc analyses of most patient-reported outcomes at month 3 (pain VAS, SF-36, Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F], European QoL-VAS) also showed a similar pattern.[61]

Ixekizumab vs. Adalimumab

We identified 1 new open-label RCT (SPIRIT H2H) for this update.[18,33,34]

This study enrolled 566 participants with active psoriatic arthritis who were naïve to biologic agents.[18,33,34] More than half of the participants in each arm used concomitant methotrexate, conventional disease modifying drugs (csDMARDs), or both.[18,33,34] Participants in each group received 1 of 2 regimens for 24 weeks; for ixekizumab, after an initial loading dose of 160 mg, participants received either 80 mg every 4 weeks or (for those who met criteria for moderate-to-severe psoriasis) 80 mg every 2 weeks from week 2 to week 12 then every 4 weeks up to week 24.[18,33,34] Adalimumab was administered either as a 40-mg starting dose then 40 mg every 2 weeks from week 2 to week 24 or (for those who met criteria for moderate-to-severe psoriasis) an 80-mg starting dose then 40 mg every 2 weeks from week 1 to week 24.[18,33,34] We rated this study moderate RoB because of the open-label design but with blinded outcome assessors and extensive manufacturer involvement in study design, execution, and reporting.

The previous review included a phase 3 RCT (SPIRIT-P1) that compared participants treated with adalimumab (40 mg every 2 weeks) with participants receiving 1 of 2 regimens of ixekizumab (80 mg every 2 weeks or 80 mg every 4 weeks, both after initial loading dose of 160 mg) or placebo.[66] The trial enrolled 417 TIM-naïve participants with moderate-to-severe psoriatic arthritis for more than 24 weeks. More than half of the participants in each arm had concomitant use of methotrexate.[66] The manufacturer of ixekizumab funded the study, and we rated it as moderate RoB because of extensive manufacturer involvement in the study design, execution, and reporting.

In the SPIRIT-P1 study, no statistical testing was conducted among the active treatment study groups because the primary study aim was to compare ixekizumab with placebo.[66] The ACR20 response rate at 24 weeks (primary study endpoint) was 57% in the adalimumab group compared

with 62% in the ixekizumab every 2 week group and 58% in the ixekizumab every 4 week group.[66] Authors observed a similar pattern of results for secondary measures of remission and improvement (ACR70, ACR50, PASI 75, PASI 90, PASI 100, and HAQ). The percentage change in BSA involvement was not different across groups (−10% vs. −11% vs. −12%).[66]

The primary outcome in the SPIRIT-H2H study was simultaneous ACR50 and PASI 100 at 24 weeks.[18] The proportion of participants achieving the primary outcome was greater in the ixekizumab group (36%) compared with the adalimumab group (28%; calculated RR, 1.3; 95% CI, 1.01 to 1.60).[18] Authors observed a similar result for PASI 100 and ACR50, but the finding for ACR50 was not statistically significant.[18] However, in a preplanned noninferiority analysis of the ACR50 response with a noninferiority margin of −12%, ixekizumab was noninferior to adalimumab.[18] Other secondary outcome measures of remission and improvement for which ixekizumab was statistically significantly better than adalimumab at 24 weeks were Minimal Disease Activity, PASI 75, PASI 90, Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC EI), DLQI, change from baseline in the modified Composite Psoriatic Disease Activity Index (mCPDAI), and change from baseline in the NAPSI.[18] Between-group differences favoring ixekizumab were maintained at 52 weeks for the primary outcome (combined ACR50 and PASI 100) and the following secondary outcomes: PASI 100, PASI 75, PASI 90, DLQI, change from baseline in the mCPDAI, and change from baseline in NAPSI.[33] There were no differences between arms for ACR50, ACR20, ACR70, NAPSI fingernails, Leeds Enthesitis Index (LEI), Leeds Dactylitis Index–Basic, and Health Assessment Questionnaire–Disability Index (HAQ-DI) at 24 weeks or 52 weeks.[18,33] In subgroup analyses, ixekizumab was more effective than adalimumab in persons with and without concomitant use of methotrexate, although the difference was not statistically significant in concomitant users.[18]

Secukinumab vs. Adalimumab

We identified 1 new multicenter, phase 3b RCT for this update (EXCEED).[16,35]

The EXCEED trial enrolled 853 participants with active psoriatic arthritis, naïve to biologic therapy for the condition, and intolerant or had inadequate response to csDMARDs.[16,35] The study compared secukinumab 300 mg administered weekly through week 4, then every 4 weeks until week 48, with adalimumab 40 mg every other week until week 50.[16,35] Participants stopped any csDMARDs and experienced a washout period of 4 weeks for all csDMARDs or 8 weeks for leflunomide.[16,35] Corticosteroids had to be maintained at a stable dose of 10 mg per day or less starting 2 weeks before randomization through the end of the study treatment period.[16,35] We rated the study moderate RoB because of differential attrition and because of extensive manufacturer involvement in study design, execution, and reporting.[16,35] The primary study endpoint was ACR20 response at 52 weeks; secondary endpoints were PASI 90, ACR50, mean change from baseline in HAQ-DI, and resolution of enthesitis measured with LEI at week 52.[16,35]

The study authors conducted 2 analyses for the primary endpoint.[16,35] The main analysis suggests no difference between arms in the proportion of participants achieving ACR20 response (secukinumab, 67%; adalimumab, 62%, calculated RR, 1.1; 95% CI, 0.98 to 1.2).[16,35] A prespecified sensitivity analysis using imputed values for missing data from nonresponders found that 67% of secukinumab recipients achieved ACR20 response compared with 59% of adalimumab recipients (calculated RR, 1.1; 95% CI, 1.02 to 1.2).[16,35] Among the secondary

outcomes, secukinumab was more effective than adalimumab as measured by PASI 90 and LEI, but ACR50 and mean change from baseline in HAQ-DI were not statistically different.[16,35] Additional analyses presented include 12 other exploratory psoriatic arthritis endpoints.[16,35] Secukinumab was more effective than adalimumab as measured by 3 of these endpoints (28-joint Disease Activity Score using C-reactive protein low disease activity, Disease Activity Index for Psoriatic Arthritis low disease activity and remission, and the Psoriatic Arthritis Response Criteria), and the other analyses found no significant differences between groups.[16,35] Three other exploratory skin endpoints were also reported; all were consistent with the PASI 90 findings.[16,35] Two other exploratory QoL endpoints were consistent with the HAQ-DI mean change score findings.[16] Findings from analyses of 211 participants with psoriatic arthritis and concomitant moderate-to-severe psoriasis found no difference between treatments in ACR20 response; however, PASI 100 response was 39% in the secukinumab group compared with 23.8% in the adalimumab group (P = .01) at week 52.[35]

Upadacitinib vs. Adalimumab

We identified 1 new RCT for this update.[26]

The Select-Psoriatic Arthritis (PsA) 1 trial compared 2 doses of upadacitinib (15 mg or 30 mg) once daily, with adalimumab 40 mg every other week.[26] The trial also included a placebo arm; the placebo comparisons are not described in this update.[26] The FDA approved dose is 15 mg daily. In the active treatment groups, there were 1,281 participants with psoriatic arthritis who were naïve to biologics and did not tolerate or had inadequate response to nonbiologic DMARDs.[26] Participants could maintain stable treatment with NSAIDs, glucocorticoids, and no more than 2 nonbiologic DMARDs, and those who did not have at least 20% improvement in tender and swollen joints at 16 weeks could initiate treatment with DMARDs, NSAIDs, acetaminophen, low-potency opioids, or glucocorticoids or adjust the dose if already receiving the drug.[26] Eighty percent or more of participants in each group were using nonbiologic DMARDs at baseline.[26] We rated this study moderate RoB because of extensive manufacturer involvement in study design, execution, and reporting. The primary study endpoint was ACR20 response at week 12 for upadacitinib compared with placebo.[26] Upadacitinib comparisons with adalimumab were analyzed by the study authors as secondary outcomes for the following measures of improvement or remission: ACR20, ACR50, ACR70, HAQ-DI, IGA 0 or 1, LEI, SF-36 PCS, FACIT-F, LDI, and Self-Assessment of Psoriasis Symptoms.[26]

Upadacitinib 30 mg was more effective than adalimumab for ACR20 response at 12 weeks (78.5% vs. 65%; calculated RR, 1.2; 95% CI, 1.1 to 1.3).[26] Similar results were observed for most secondary outcomes. Authors reported no difference between upadacitinib 15 mg and adalimumab for most outcomes.[26]

Ustekinumab vs. TNF-α Inhibitors

We did not identify any new RCTs for this update.

The previous review included 1 RCT[43] enrolling 47 participants with psoriatic arthritis and active enthesitis. The authors describe the study design as a "prospective observational trial"; however, authors reported that participants were randomized to either 45 mg or 90 mg of ustekinumab (depending on body weight) at weeks 0, 4, 12, and 24, or to standard approved doses of TNF-α

inhibitors (the selection of TNF-α inhibitor was left up to the participant based on preferred route and frequency of administration). German governmental agencies funded this study.[43] We rated this study high RoB because of the paucity of information related to randomization and allocation concealment, self-selection of agents in the TNF-α inhibitors comparison group, and the lack of blinding among participants and investigators. The primary study endpoint was a change in the SPARCC EI and complete remission (0 on the SPARCC EI) at week 24.[43] Authors evaluated numerous secondary endpoints, including other measures of enthesitis (question 4 on the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], LEI, Maastricht Ankylosing Spondylitis Enthesitis Score [MASES]), measures of arthritis (Bath Ankylosing Spondylitis Function Index [BASFI], swollen joint count, tender joint count, Disease Activity Index for Psoriatic Arthritis, VAS pain and global disease), skin and nail involvement (PASI 90, PASI 100, NAPSI), functional impairment and related symptoms (HAQ, FACIT-F), and QoL (SF-36 PCS and MCS).[43]

Ustekinumab was superior to TNF-α inhibitors for achieving complete enthesitis remission at 24 weeks as measured by SPARCC EI score of 0 (74% vs. 42%; *P* = .02).[43] Authors observed similar findings on other measures of enthesitis (LEI, MASES, question 4 of BASDAI). No significant differences were observed in achieving complete remission of arthritis symptoms as measured by tender or swollen joint count.[43] Ustekinumab-treated participants had a larger response on measures of psoriasis activity in skin (PASI 100, 50% vs. 29%; *P* = .04) and nails, and in the PCS component of the SF-36 (but not the MCS component).[43]

Table 9. Evidence Table for Efficacy Outcomes in Adults for TIMs for Psoriatic Arthritis (Brief Version)

Authors, Year Trial Name	Study Design	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Adalimumab vs. etanercept vs. infliximab									
Atteno et al., 2010[50]	RCT	100	12 months	Adalimumab 40 mg every 2 weeks vs. etanercept 25 mg twice weekly vs. infliximab 5 mg/kg every 6 to 8 weeks	HAQ, PASI, TJC, SJC, ACR20, AEs[a]		Adults with psoriatic arthritis with an inadequate response to DMARDs	Similar ACR20, HAQ, TJC, SJC response rates between groups; some differences in median PASI response	High
Adalimumab vs. tofacitinib									
Mease et al., 2017[60] OPAL Broaden	RCT	422	12 months	Adalimumab 40 mg every 2 weeks vs. tofacitinib 5 mg twice daily vs. tofacitinib 10 mg twice daily	ACR20, HAQ	ACR50/70, PASI 75, LEI, BSA, mTSS, DAS28-CRP, FACIT-F, SF-36, EQ-VAS	Adults with psoriatic arthritis with an inadequate response to DMARDs	Numerically highest responses across measures for tofacitinib 10 mg group, but no statistical testing conducted[d]	Moderate
Ixekizumab vs. adalimumab									
Mease et al., 2020[18] Smolen et al., 2020[33] Smolen et al., 2020[34] SPIRIT-H2H	Open-label RCT	566	52 weeks	Ixekizumab 80 mg every 4 weeks vs. adalimumab 40 mg every 2 weeks	ACR50 and PASI 100	ACR20/50/70, PASI 75/90/100, MDA, mCPDAI, SPARCC, LEI, LDI-B, NAPSI, HAQ-DI, DLQI	Adults with active psoriatic arthritis for at least 6 months and with active plaque psoriasis	Ixekizumab was more effective than adalimumab for improving skin disease and was similarly effective for improving joint disease	Moderate

Authors, Year Trial Name	Study Design	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Mease et al., 2017[66] SPIRIT-P1	RCT	417	24 weeks	Ixekizumab 80 mg every 2 weeks[b] vs. ixekizumab 80 mg every 4 weeks[b] vs. adalimumab 40 mg every 2 weeks	ACR20	ACR50/70, BSA, HAQ, mTSS, DAS28-CRP, PASI 75/90/100	TIM-naïve adults with active psoriatic arthritis	Numerically highest responses across measures for ixekizumab every 2 weeks, followed by ixekizumab every 4 weeks, then adalimumab but no statistical testing conducted[c]	Moderate
Secukinumab vs. adalimumab									
McInnes et al., 2020[16] Gottlieb et al.,[35] 2021 EXCEED	RCT	853	52 weeks	Secukinumab 300 mg every 4 weeks vs. adalimumab 40 mg every 2 weeks	ACR20	ACR50, PASI 90, HAQ-DI, LEI	TIM-naïve adults with active psoriatic arthritis with an inadequate response to csDMARDs	No significant difference in ACR20 response, ACR50, HAQ-DI score, and resolution of enthesitis between secukinumab and adalimumab. Secukinumab was more effective than adalimumab on PASI 90.	Moderate

Authors, Year Trial Name	Study Design	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Upadacitinib vs. adalimumab									
McInnes et al., 2021[26] SELECT-PsA 1	RCT	1,281 (excluding placebo group)	24 weeks	Upadacitinib 15 mg once daily vs. upadacitinib 30 mg once daily vs. adalimumab 40 mg every other week	ACR20 (vs. placebo)	ACR50/70, HAQ-DI, sIGA 0 or 1, LEI, SF-36 PCS, FACIT-F, LDI, Self-Assessment of Psoriasis Symptoms (vs. placebo or vs. adalimumab)	Adults with psoriatic arthritis and historical or current plaque psoriasis	Upadacitinib 30 mg was more effective than adalimumab on the primary outcome and most secondary outcomes; no difference on most outcomes for 15 mg upadacitinib	Moderate
Ustekinumab vs. TNF-α inhibitor									
Araujo et al., 2019[43] ECLIPSA	RCT	47	24 weeks	Ustekinumab 45 mg or 90 mg[e] vs. TNF-α inhibitor per patient's choice at standard approved doses	SPARCC EI change, SPARCC EI 0	MASES, LEI, PASI 90/100,TJC, SJC, DAS, DAPSA, NAPSI, BASDAI, BASFI, VAS pain and global disease activity, SF-36 PCS and MCS, HAQ, FACIT-F	Adults with psoriatic arthritis with active enthesitis	Ustekinumab more effective than TNF-α inhibitor therapy on measures of enthesitis and skin disease, no significant differences on measures of arthritis	High

Authors, Year Trial Name	Study Design	Number of Participants	Duration	Comparisons	Primary Outcome	Secondary Outcomes	Population	Results	Risk of Bias
Bimekizumab (pipeline drug) vs. placebo									
Ritchlin et al., 2020[20] BE ACTIVE	RCT	206 (including all dose groups, 83 if only considering 320 mg and placebo groups)	12 weeks (double-blind portion)	Bimekizumab 320 mg vs. placebo	ACR50	ACR20/70, PASI 75/90, MASES, HAQ-DI, PsAID ≤ 3	Adults with active adult-onset psoriatic arthritis for at least 6 months and an active psoriatic skin lesion	Bimekizumab more effective than placebo as measured by some (ACR20/50, PASI 75/90, HAQ-DI, SF-36 PCS, PsAID < 3) but not all outcomes	Moderate

Notes. [a] Article did not distinguish between primary and secondary outcomes. [b] After an initial loading dose of 160 mg at week 0. [c] The primary study aim was to compare ixekizumab to placebo; statistical significance testing between active arms was not conducted. [d] The primary study aim was to compare tofacitinib to placebo; statistical significance testing between active arms was not conducted. [e] Dosage was 45 mg if body weight was ≤ 100 kg and dose was 90 mg if body weight > 100 kg.

Abbreviations. ACR: American College of Rheumatology percentage improvement; AE: adverse event; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Function Index; BSA: percentage of psoriasis-affected body surface area; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS: Disease Activity Score; DAS28-CRP: 28-joint Disease Activity Score using C-reactive protein; DLQI: Dermatology Life Quality Index; DMARD: disease-modifying antirheumatic drug; EQ-VAS: European QoL-Visual Analog Scale; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ: Health Assessment Questionnaire; HAQ-DI: Health Assessment Questionnaire–Disability Index; LDI-B: Leeds Dactylitis Index—Basic; LEI: Leeds Enthesitis Index; MASES: Maastrict Ankylosing Spondylitis Enthesitis Score; mCPDAI: modified Composite Measures of Disease Activity in Psoriatic Arthritis; MDA: Minimal Disease Activity; mTSS: modified Total Sharp Score; NAPSI: Nail Psoriasis Severity Index; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PsAID: Psoriatic Arthritis Impact of Disease; PsA: psoriatic arthritis; NRS: Numeric Rating Scale; RCT: randomized controlled trial; SF-36: short form survey; SF-36 MCS: Short Form Survey Mental Health Component Score; SF-36 PCS: Short Form Survey Physical Health Component Score; sIGA: static Investigator Global Assessment; SJC: swollen joint count; SPARCC EI: Spondylarthritis Research Consortium of Canada Enthesitis Index; TIM: targeted immune modulator; TJC: tender joint count; TNF-α: tumor necrosis factor alpha; VAS: visual analog scale; vs.: versus.

Comparative Harms (KQ2)

Six RCTs[16,18,26,50,60,66] that reported efficacy outcomes for KQ1 also reported comparative harm outcomes. In addition, 1 cohort study reported harm outcomes.[56]

Harms Reported in RCTs

Table 10 summarizes high-level findings for harms from 6 RCTs that reported these outcomes. Detailed findings are summarized in Table 11. Overall, we observed very few differences in head-to-head comparisons of TIM agents for overall AEs, SAEs, and withdrawals due to AEs.

Table 10. Summary of AEs from RCTs in Adults Receiving TIMs for Psoriatic Arthritis

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Adalimumab vs. infliximab vs. etanercept				
Atteno et al., 2010[50]	100	12 months	Incidence of AEs (23% vs. 17% vs. 6%, $P < .001$); adalimumab with significantly lower incidence of AEs than either etanercept or infliximab; infliximab with significantly higher incidence of AEs than etanercept. Withdrawals due to AEs, NR; 2 SAEs reported overall, both in the infliximab group. Injection-site/infusion reactions NR.	High
Adalimumab vs. tofacitinib				
Mease et al., 2017[60] OPAL Broaden	422	12 months	No significant differences in AEs, SAEs, or withdrawals due to AEs.	Moderate
Ixekizumab vs. adalimumab				
Mease et al., 2020[18] Smolen et al., 2020[33] Smolen et al., 2020[34] SPIRIT-H2H	566	52 weeks	Fewer SAEs but more injection-site reactions with ixekizumab vs. adalimumab; no significant differences in withdrawals due to AEs or overall AEs.	Moderate
Mease et al., 2017[66] SPIRIT-P1	417	24 weeks	Injection-site/infusion reactions more frequent with ixekizumab (2.0% vs. 13.9%; RR, 0.14; 95% CI, 0.03 to 0.59). No significant differences in overall AEs, SAEs, or withdrawals due to AEs.	Moderate
Secukinumab vs. adalimumab				
McInnes et al., 2020[16] Gottlieb et al., 2021[35] EXCEED	853	52 weeks	Withdrawals due to AE and injection/infusion site reactions were less frequent with secukinumab (4% vs. 7%; calculated RR, 0.53; 95% CI, 0.30 to 0.94 and 4% vs. 11%; calculated RR, 0.36; 95% CI, 0.21 to 0.62). No significant differences in overall AEs and SAEs.	Moderate

Authors, Year Trial Name	Number of Participants	Duration	Results	Risk of Bias
Upadacitinib vs. adalimumab				
McInnes et al., 2021[26] SELECT-PsA 1	1,281 (excluding placebo group)	24 weeks	Higher risk of AEs and SAEs for upadacitinib 30 mg than adalimumab . No significant differences in withdrawals due to AEs with 15-mg dosage.	Moderate
Bimekizumab (pipeline drug) vs. placebo				
Ritchlin et al., 2020[20] BE ACTIVE	83 if only considering 320 mg and placebo groups	12 weeks	No significant differences in AEs, SAEs or discontinuations due to AEs.	Moderate

Abbreviations. AE: adverse event; CI: confidence interval; NR: not reported; RCT: randomized controlled trial; RR: risk ratio; SAE: serious adverse event; TIM: targeted immune modulator; vs.: versus.

Table 11. Comparisons of TIMs in RCTs for General Tolerability in Adults With Psoriatic Arthritis

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawals Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/ Infusion Reactions: RR (95% CI)	Risk of Bias
Adalimumab vs. infliximab vs. etanercept						
Atteno et al., 2010[50]	100 12 months	Adalimumab vs. etanercept: 0.38 (0.17 to 0.84) Adalimumab vs. infliximab: 0.23 (0.11 to 0.49) Infliximab vs. etanercept: 1.6 (1.1 to 2.4)	NR	2 events in the infliximab group	NR	High
Adalimumab vs. tofacitinib						
Mease et al., 2017[60] OPAL Broaden	422 12 months	1.1 (0.90 to 1.3)	0.67 (0.20 to 2.3)	1.14 (0.46 to 2.8)	NA (oral agent)	Moderate
Ixekizumab vs. adalimumab						
Mease et al., 2020[18] Smolen et al., 2020[33] Smolen et al., 2020[34] SPIRIT-H2H	566 52 weeks	1.1 (0.97 to 1.2)	0.57 (0.29 to 1.1)	0.34 (0.18 to 0.65)	3.0 (1.5 to 6.02)	Moderate
Mease et al., 2017[66] SPIRIT-P1	417 24 weeks	1.0 (0.83 to 1.3) for every 2-wk dosage	2.0 (0.37 to 10.6) for every 2-wk dosage	0.59 (0.15 to 2.4) for every 2-wk dosage	7.9 (1.9 to 33.6) for every 2-wk dosage	Moderate
Secukinumab vs. adalimumab						
McInnes et al., 2020[16] Gottlieb et al., 2021[35] EXCEED	853 52 weeks	0.98 (0.91 to 1.1)	0.53 (0.30 to 0.94)	1.1 (0.70 to 1.9)	0.36 (0.21 to 0.62)	Moderate

Authors, Year Trial Name	Number of Participants Duration	Overall AEs: RR (95% CI)	Withdrawals Due to AEs: RR (95% CI)	SAEs: RR (95% CI)	Injection-Site Reactions/ Infusion Reactions: RR (95% CI)	Risk of Bias
Upadacitinib vs. adalimumab						
McInnes et al., 2021[26] SELECT-PsA 1	1,281 (excluding placebo group) 24 weeks	15 mg: 1.03 (0.94 to 1.1) 30 mg: 1.1 (1.02 to 1.2)	15 mg: 0.59 (0.30 to 1.2) 30 mg: 0.97 (0.54 to 1.7)	15 mg: 0.88 (0.43 to 1.8) 30 mg: 1.6 (0.90 to 3.02)	NR	Moderate
Bimekizumab (pipeline drug) vs. placebo						
Ritchlin et al., 2020[20] BE ACTIVE	83 if only considering 320 mg and placebo groups 12 weeks	0.85 (0.57 to 1.3)	NA (0 events in 1 group)	NA (0 events in 1 group)	NR	Moderate

Notes: All entries in this table are calculated values from the data provided in the articles.
Abbreviations. AE: adverse event; CI: confidence interval; mg: milligram; NA: not applicable; NR: not reported; RCT: randomized controlled trial; RR: risk ratio; SAE: serious adverse event; TIM: targeted immune modulator; vs.: versus; wk: week.

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Harms Reported in Cohort Studies

We identified no new cohort studies focused specifically on individuals with psoriatic arthritis. The previous review included 1 high-RoB cohort study[56]; this study is summarized in Table 12. Kisacik and colleagues identified patients with various rheumatologic conditions, including psoriatic arthritis, from a Turkish patient registry.[56] Study authors reported a significantly higher risk for tuberculosis with infliximab (1.3%) compared with etanercept (0.3%) or adalimumab (0.6%).[56]

Table 12. Summary of Observational Studies of AEs in Adults Receiving TIMs for Psoriatic Arthritis

Authors, Year	Number of Participants	Follow-up	Comparison[a]	Population	Results	Risk of Bias
Kisacik et al., 2016[56]	10,434	NR	Adalimumab vs. etanercept vs. infliximab	Ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, Behcet disease identified through a patient a Turkish patient registry	Significantly higher risk for tuberculosis with infliximab than etanercept or adalimumab	High

Note. [a] Dosages not reported.
Abbreviations. AE: adverse event; NR: not reported; TIM: targeted immune modulator.

Efficacy and Harms of Pipeline TIM Agents for Psoriatic Arthritis

We identified 1 new RCT[20] for this update that reported on the efficacy and harms of the pipeline TIM agent bimekizumab. Table 13 shows the Summary of Findings (GRADE) for the comparison of bimekizumab with placebo. Tables 9, 10, and 11 provide a summary of this evidence base and summarize the findings. Appendix B, Tables B1 and B2 provide detailed study characteristics and results, and Appendix D describes efficacy outcome measures used. We rated this RCT moderate RoB because of extensive manufacturer involvement in study design, execution, and reporting.

Table 13. Summary of Findings (GRADE) of Pipeline TIMs in Adults for Psoriatic Arthritis

Outcome	Certainty of Evidence	Relationship[a]
Bimekizumab vs. placebo[b]		
Clinical improvement (1 RCT)	⨁⨁◯◯ (low)	Favors bimekizumab
QoL (1 RCT)	⨁⨁◯◯ (low)	Favors bimekizumab
AEs (1 RCT)	⨁◯◯◯ (very low)	No difference
SAEs (1 RCT)	⨁◯◯◯ (very low)	Unable to determine

Note. [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] New comparison for this update.
Abbreviations. AE: adverse event; GRADE: Grading of Recommendations, Assessment, Development, and Evaluation approach; QoL: quality of life; RCT: randomized controlled trial; SAE: serious adverse event; TIM: targeted immune modulator.

Bimekizumab vs. Placebo

We identified 1 new moderate-RoB phase 2b RCT for this update, the BE ACTIVE trial.[20]

This study enrolled 206 participants and compared 4 dosages of bimekizumab with placebo.[20] Participants received assigned treatments every 4 weeks for 16 weeks.[20] Bimekizumab was administered as either: 16 mg; 160 mg; a starting dose of 320 mg followed by 160 mg; and 320 mg.[20] Only the bimekizumab 320 mg and placebo comparison is summarized in this update because it is the only dose within the range that will be evaluated for FDA approval; there were 83 participants randomized to those 2 groups.[20] The primary study endpoint was ACR50. Secondary endpoints included ACR20, ACR70, PASI 75, PASI 90, MASES, HAQ-DI, and Psoriatic Arthritis Impact of Disease score of 3 or lower.[20]

Bimekizumab 320 mg was more effective than placebo for the primary endpoint (ACR50; calculated RR, 3.4; 95% CI, 1.01 to 11.50), and the following secondary endpoints: ACR20, PASI 90, PASI 75, Psoriatic Arthritis Impact of Disease score of 3 or lower, and mean change from baseline in HAQ-DI and SF-36 PCS.[20] Other measures, including harms such as AEs, SAEs, and discontinuations because of AEs, were no different between groups.[20]

Evidence for Subgroups

Few studies reported findings for subgroups of interest for this update (KQ3). This section summarizes relevant subgroup findings presented in earlier sections for head-to-head RCT comparisons of agents for plaque psoriasis and for psoriatic arthritis.

- *Brodalumab vs. ustekinumab for plaque psoriasis*: No differences were found in comparative efficacy or safety in post hoc subgroup analysis of participants with BMI < 30 kg/m^2 versus those with BMI ≥ 30 kg/m^2.[76]
- *Guselkumab vs. secukinumab for plaque psoriasis*: Guselkumab was superior to secukinumab overall and in all subgroups evaluated based on age, weight, BMI, severity of disease, body area affected, and prior medication use.[80]
- *Ixekizumab vs. adalimumab for psoriatic arthritis*: Ixekizumab was more effective than adalimumab in persons with and without concomitant use of methotrexate, although the difference was not statistically significant in concomitant users.[18]
- *Tildrakizumab vs. etanercept for plaque psoriasis*: No differences were found in efficacy observed for participants with metabolic syndrome compared with those without metabolic syndrome.[75]

Ongoing Studies

We identified 17 ongoing studies[89-105] (12 RCTs and 5 cohort studies) evaluating the comparative effectiveness or harms of TIM agents (Tables 14, 15, and 16). Six RCTs[89-94] are in participants with plaque psoriasis and 6 RCTs[95-100] are in participants with psoriatic arthritis. Three cohort studies are in participants with plaque psoriasis,[101,103,104] 1 is in participants with psoriatic arthritis,[102] and 1 study includes participants with either condition.[105] Drug manufacturers are funding 16 studies[89-101,103-105] and hospitals are funding 1 study.[102]

Table 14. Ongoing RCTs of TIMs for Plaque Psoriasis

Trial Number Trial Name Phase	Treatment Groups Blinded vs. Open Label	Estimated Enrollment Treatment Duration	Estimated Study Completion Date[a]	Primary Outcome(s)
Bimekizumab vs. placebo				
NCT05020249[89] A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Bimekizumab in Adult Korean Study Participants With Moderate to Severe Plaque Psoriasis Phase 3	Bimekizumab, placebo Blinded	N = 45 16 weeks	October 2022	• PASI 90 • IGA (0,1)
Brodalumab vs. guselkumab				
NCT04533737[90] Efficacy and Safety of Brodalumab Compared With Guselkumab in the Treatment of Plaque Psoriasis After Inadequate Response to Ustekinumab (COBRA) Phase 4	Brodalumab, guselkumab, placebo Blinded	N = 260 28 weeks	October 2022	• PASI 100
Deucravacitinib vs. placebo				
NCT04167462[91] An Investigational Study to Evaluate Experimental Medication BMS-986165 Compared to Placebo in Participants With Plaque Psoriasis (POETYK-PSO-3) in Mainland China, Taiwan, and South Korea Phase 3	Deucravacitinib, placebo Blinded	N = 220 (actual) 16 weeks	December 2021 (actual)	• PGA (0,1) • PASI 75
Deucravacitinib vs. apremilast				
NCT03611751[92] An Investigational Study to Evaluate Experimental Medication BMS-986165 Compared to Placebo and a Currently Available Treatment in Participants With Moderate-to-Severe Plaque Psoriasis (POETYK-PSO-2) Phase 3	Deucravacitinib, apremilast, placebo Blinded	N = 1,020 (actual) 16 weeks	November 2020 (actual)	• PGA (0,1) • PASI 75
NCT03624127[93] A Multi-Center, Randomized, Double-Blind, Placebo- and Active Comparator-Controlled Phase 3 Study to Evaluate the Efficacy and Safety of BMS-986165 in Subjects With Moderate-to-Severe Plaque Psoriasis (POETYK-PSO-1) Phase 3	Deucravacitinib, apremilast, placebo Blinded	N = 666 (actual) 16 weeks	September 2020 (actual)	• PGA (0,1) • PASI 75

Trial Number Trial Name Phase	Treatment Groups Blinded vs. Open Label	Estimated Enrollment Treatment Duration	Estimated Study Completion Date[a]	Primary Outcome(s)
Risankizumab vs. apremilast				
NCT04908475[94] Study of Subcutaneous Risankizumab Injection Compared to Oral Apremilast Tablets to Assess Change in Disease Activity and Adverse Events in Adult Participants With Moderate Plaque Psoriasis Who Are Candidates for Systemic Therapy	Risankizumab, apremilast Blinded	N = 330 16 weeks	April 2023	• PASI 90 • PGA (0,1)

Notes. [a] *As reported in ClinicalTrials.gov registry.*
Abbreviations. IGA: Investigator's Global Assessment; N: number of participants; NCT: US National Clinical Trial; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PGA: Physician's Global Assessment; RCT: randomized controlled trial; TIM: targeted immune modulator; vs.: versus.

Table 15. Ongoing RCTs of TIMs for Psoriatic Arthritis

Registration Number Trial Name Phase	Treatment Groups; Blinded vs. Open Label	N Enrollment Treatment Duration	Study Completion Date[a]	Primary Outcome(s)
Bimekizumab vs. placebo				
NCT03896581[95] A Study to Evaluate the Efficacy and Safety of Bimekizumab in the Treatment of Subjects With Active Psoriatic Arthritis (BE COMPLETE) Phase 3	Bimekizumab, placebo Blinded	N = 400 16 weeks	March 2022	ACR50
Bimekizumab vs. adalimumab[b]				
NCT03895203[96] A Study to Test the Efficacy and Safety of Bimekizumab in the Treatment of Subjects With Active Psoriatic Arthritis (BE OPTIMAL) Phase 3	Bimekizumab, adalimumab, placebo Blinded	N = 852 16 weeks	August 2022	ACR50

Registration Number Trial Name Phase	Treatment Groups; Blinded vs. Open Label	N Enrollment Treatment Duration	Study Completion Date[a]	Primary Outcome(s)
Deucravacitinib vs. placebo				
NCT04908202[97] A Study to Determine the Efficacy and Safety of Deucravacitinib Compared With Placebo in Participants With Active Psoriatic Arthritis (PsA) Who Are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs Phase 3	Deucravacitinib, placebo Blinded	N = 650 16 weeks	July 2024	ACR20
NCT03881059[98] Efficacy and Safety of BMS-986165 Compared With Placebo in Participants With Active Psoriatic Arthritis (PsA) Phase 2	Deucravacitinib, ustekinumab, placebo Blinded	N = 203 (actual) 16 weeks	January 2021 (actual)	ACR20
Deucravacitinib vs. apremilast				
NCT04908189[99] A Study to Determine the Efficacy and Safety of Deucravacitinib Compared With Placebo in Participants With Active Psoriatic Arthritis (PsA) Who Are Naïve to Biologic Disease Modifying Anti-rheumatic Drugs or Had Previously Received TNFα Inhibitor Treatment Phase 3	Deucravacitinib, apremilast, placebo Blinded	N = 700 16 weeks	July 2024	ACR20
Secukinumab vs. adalimumab				
NCT04632927[100] Efficacy of Secukinumab Compared to Ustekinumab in Adults With Active Psoriatic Arthritis and Failure of TNF-α Inhibitor Treatment (AgAIN) Phase 3	Secukinumab, adalimumab Blinded	N = 310 28 weeks	April 2023	HAQ-DI

Notes. [a] As reported in ClinicalTrials.gov registry. [b] Study included participants with both plaque psoriasis and psoriatic arthritis.
Abbreviations. ACR: American College of Rheumatology percentage improvement; HAQ-DI: Health Assessment Questionnaire–Disability Index; N: number of participants; NCT: US National Clinical Trial; RCT: randomized controlled trial; TIM: targeted immune modulator; TNF-a: tumor necrosis factor alpha; vs.: versus.

Table 16. Ongoing Cohort Studies of TIMs for Plaque Psoriasis or Psoriatic Arthritis

Trial Number Trial Name	Treatment Groups	N Enrollment Treatment Duration	Study Completion Date[a]	Primary Outcome(s)
NCT04799990[101] Study to Assess Adverse Events When Subcutaneous Risankizumab Injection is Given to Adult Participants With Psoriasis in Real World Setting	• Risankizumab • Biological Comparator 1 (biologics other than IL-23 antagonists) • Drug Comparator 2 (nonbiologic systemic small molecules)	N = 6,000 Up to 10 years	October 2030	• Major cardiovascular events
NCT01965132[102] Korean College of Rheumatology Biologics Registry KOBIO	• Etanercept • Adalimumab • Infliximab • Golimumab • Tocilizumab • Abatacept • Rituximab • Ustekinumab • Secukinumab	N = 7,000 (Estimated) Up to 10 years	June 2025	• AEs
NCT02075697[103] Spanish Registry of Systemic Treatments in Psoriasis BIOBADADERM	• Biologic therapy, apremilast of fumarates • Nonbiological systemic treatment (methotrexate, cyclosporine and acitretin)	N = 3,500 5 years	October 2025	• SAEs
NCT00508547[104] Psoriasis Longitudinal Assessment and Registry PSOLAR	• Guselkumab • Infliximab • Ustekinumab • Biological therapies other than infliximab, ustekinumab, and guselkumab • Conventional systemic agents	N = 16,000 8 years	December 2031	• AEs • SAEs
NCT01848028[105] PsoBest – The German Psoriasis Registry	• Fumaric acid ester • Methotrexate • Cyclosporine A • Etanercept • Infliximab • Adalimumab • Ustekinumab • Golimumab • Secukinumab • Apremilast • Certolizumab • Retinoids • Leflunomides • Systemic PUVA	N = 3,500 10 years	July 2026	• PASI

Notes. [a] As reported in ClinicalTrials.gov registry.
Abbreviations. AE: adverse event; IL: interleukin; N: number of participants; NCT: US National Clinical Trial; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PUVA: psoralen and ultraviolet A; SAE: serious adverse event; TIM: targeted immune modulator.

Discussion

For plaque psoriasis, the largest body of comparative evidence continues to be for etanercept and ustekinumab compared with other TIM agents, although new studies are available in this update for ixekizumab, secukinumab, and risankizumab. For clinical improvement and disease remission outcomes, there is moderate and high CoE to suggest etanercept is less effective than certolizumab pegol, ixekizumab, secukinumab, and tildrakizumab. There is very low to low CoE to suggest etanercept is less effective than ustekinumab and probably not significantly different compared with apremilast. There is moderate and high CoE to suggest ustekinumab is less effective than brodalumab, risankizumab, ixekizumab, and secukinumab.

Several other head-to-head comparisons are available. There is moderate and high CoE to suggest guselkumab is more effective than adalimumab and also more effective than secukinumab at later (but not earlier) time points; guselkumab is less effective at early time points compared with ixekizumab, but no difference is observed between these agents at later time points. There is moderate CoE to suggest no difference between ixekizumab and secukinumab. There is moderate CoE to suggest risankizumab is more effective than adalimumab and more effective than secukinumab at later but not earlier time points. QoL outcomes typically mirrored clinical improvement and disease remission outcomes in most, but not all, studies.

With 1 exception, comparisons with at least low CoE did not identify any differences between agents in AEs or SAEs for any head-to-head comparisons.

There is moderate and high CoE to suggest the 2 pipeline TIM agents included in this report (bimekizumab, deucravacitinib) are more effective compared with placebo, but with more AEs. Further, bimekizumab is also more effective than adalimumab, secukinumab, and ustekinumab on measures of disease remission and QoL (moderate-quality evidence) with no difference in AEs (moderate CoE) or SAEs (low CoE).

For psoriatic arthritis, limited head-to-head comparisons were available. Ixekizumab, secukinumab, and upadacitinib may be more effective than adalimumab for improving skin symptoms (moderate CoE), but only higher doses of upadacitinib were more effective at also improving arthritis symptoms. There is very low to moderate CoE to suggest that, compared with adalimumab, no difference in harms exists for tofacitinib, ixekizumab, or secukinumab, but upadacitinib has more AEs. There is low CoE for 1 pipeline agent to suggest that bimekizumab is more effective for clinical improvement and QoL than placebo, with no difference in AEs (very low CoE).

Data From Network Meta-analyses

In this section, we briefly summarize findings from recent network meta-analyses that included RoB assessments for included studies.

In a 2021 Cochrane network meta-analysis conducted by Sbidian and colleagues, authors evaluated the following agents for plaque psoriasis relevant to this DERP update: adalimumab, apremilast, bimekizumab, brodalumab, certolizumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, tofacitinib, and ustekinumab, in addition to several other biologic agents (not included in this update) and conventional, nonbiologic

agents.[137] All agents were superior to placebo as evaluated by the PASI 90 outcome. Several differences were observed among drug classes and drugs[137]:

- The anti-IL and anti-TNF-α agents were superior to the small molecule agents (i.e., apremilast, tofacitinib)
- Infliximab, anti-IL-17 drugs (bimekizumab, brodalumab, ixekizumab, and secukinumab) and the anti-IL-23 drugs (guselkumab and risankizumab, but not tildrakizumab) were more effective than adalimumab, certolizumab, etanercept, and ustekinumab
- Adalimumab and ustekinumab were more effective than certolizumab and etanercept

The authors concluded that brodalumab, guselkumab, infliximab, ixekizumab, risankizumab, and secukinumab were the most effective choices, based on moderate-to-high CoE.[137] However, these findings were limited to initial therapy; evidence for longer-term maintenance therapy was limited.[137] Another recently published network meta-analysis reported similar findings related to efficacy.[138]

One network meta-analysis published in 2021 specifically focused on safety outcomes and the risk-benefit profile.[139] It concluded that in the long term, risankizumab had the lowest rates of AEs, SAEs, and discontinuations due to AEs, and the most favorable benefit-risk profile.[139]

With respect to psoriatic arthritis, we identified several recent network meta-analyses. In a 2020 network meta-analysis, authors observed few significant differences between agents, which included abatacept, adalimumab, apremilast, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, secukinumab, tofacitinib, and ustekinumab.[140] Based on the ACR outcome, all treatments were superior to placebo except abatacept.[140] The most effective agent was infliximab, followed by golimumab and etanercept.[140] Ixekizumab was more effective than abatacept, apremilast, and ustekinumab.[140] However, these findings were not consistent with findings as evaluated using the PsARC outcome.[140] In another network meta-analysis also published in 2020, authors reported findings based on ACR outcome and reported similar results.[141]

Limitations of the Evidence

Although the evidence base for head-to-head comparisons of TIM agents includes numerous studies, few comparisons were evaluated by more than 1 or 2 studies. Furthermore, gaps remain for specific head-to-head comparisons because of the number of TIM agents that are available. Most RCTs were focused on efficacy outcomes after induction, typically 12 to 16 weeks in, and fewer reported outcomes from maintenance therapy. Drug manufacturers sponsored nearly all included RCTs. Although the extent to which the manufacturer's involvement influenced study execution or reporting is not definitively known, findings from a Cochrane systematic review suggest that industry sponsorship is associated with more favorable results than sponsorship by other sources.[142] Several of the cohort studies we included used administrative or claims data to evaluate harms, and the validity of this approach for evaluating harms is uncertain. The bodies of evidence for both plaque psoriasis and psoriatic arthritis were often downgraded by 1 or 2 levels for imprecision and, in some cases, for study limitations also. Further, several studies in this body of evidence were primarily designed to assess effectiveness compared with a placebo control and were not designed to evaluate comparative effectiveness.

Limitations of This Review

This review has several limitations. First, we did not include RCTs shorter than 12 weeks in duration, cohort studies with fewer than 1,000 participants, or studies published in languages other than English. We included only studies published in the peer-reviewed literature; we did not use data presented in press releases or conference abstracts. This review represents a cumulative synthesis of the evidence. Thus, studies included in the prior DERP review on this topic were carried forward into this update if they continued to meet eligibility criteria; however, data from these studies were not rechecked against the original sources for accuracy. Further, we did not reevaluate the RoB for the previously included studies.

Conclusions

In conclusion, for clinical improvement and disease remission outcomes in plaque psoriasis, there is moderate and high CoE to suggest etanercept is less effective than certolizumab pegol, ixekizumab, secukinumab, and tildrakizumab. There is also moderate and high CoE to suggest ustekinumab is less effective than brodalumab, ixekizumab, risankizumab, and secukinumab. Other comparisons with moderate or high CoE for clinical improvement and disease remission favor guselkumab: a) versus adalimumab; b) versus secukinumab (at later time points); and c) versus ixekizumab (at early but not later time points). There is moderate CoE to suggest no difference between ixekizumab and secukinumab. There is moderate CoE for the favoring of risankizumab versus adalimumab and versus secukinumab (at later time points). Few differences in harms among TIM agents were observed, based on very low to moderate CoE.

For psoriatic arthritis, limited head-to-head comparisons are available. The only moderate-certainty head-to-head evidence compared ixekizumab, secukinumab, or upadacitinib with adalimumab; all were superior to adalimumab for improving skin disease, but only higher doses of upadacitinib were superior for improving arthritis symptoms. However, upadacitinib had more AEs compared with adalimumab. Few other differences in harms among TIM agents were observed, based on very low to moderate CoE.

The ongoing studies we identified for plaque psoriasis and psoriatic arthritis will address some gaps in the evidence by evaluating new comparisons or potentially increasing our CoE for existing comparisons. When reviewing this report, state Medicaid administrators might consider using the findings and conclusions as a tool in their evidence-based decision-making process, such as for clarifying place in therapy for TIM agents and populations of interest.

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Appendix A. Clinical Evidence Methods

Search Strategy

We searched Drug Effectiveness Review Project (DERP) clinical evidence sources to identify randomized controlled trials (RCTs), and cohort studies (for harms) using terms for the conditions (*plaque psoriasis*, *psoriatic arthritis*) and the interventions (*abatacept*, *adalimumab*, *apremilast*, *brodalumab*, *certolizumab pegol*, *etanercept*, *golimumab*, *guselkumab*, *infliximab*, *ixekizumab*, *secukinumab*, *tildrakizumab*, *tofacitinib*, *ustekinumab*, *risankizumab*, *upadacitinib*, *bimekizumab*, *BMS-986165*, *deucravacitinib*) and study design limits. We limited searches of evidence sources to citations published between May 1, 2019, and August 25, 2021. We conducted active surveillance of known ongoing studies through December 31, 2021.

We searched the following DERP evidence sources:

- Agency for Healthcare Research and Quality
  - Evidence-based Practice Centers Reports
  - Effective Health Care Program
- Canadian Agency for Drugs and Technologies in Health
- Cochrane Library (Wiley Interscience)
- National Institute for Health and Care Excellence, Evidence
- MEDLINE via PubMed
- Veterans Administration Evidence-based Synthesis Program

MEDLINE via PubMed Search Strategy

May 1, 2019, to August 25, 2021

Psoriasis Terms

#1 ("Psoriasis"[Mesh] OR psoriasis[Text Word] OR psoriatic arthr*[Text Word]) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Drug Terms

#2 ("Biological Products"[Mesh:NoExp] OR biologic therap*[Title/Abstract] OR biologics[Title/Abstract] OR "Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh] OR tumor necrosis factor alpha inhibitor*[Title/Abstract] OR anti-tumor necrosis factor alpha[Title/Abstract] OR tumor necrosis factor alpha block*[Title/Abstract] OR tumor necrosis factor alpha antagonist*[Title/Abstract] OR TNF-alpha inhibitor*[Title/Abstract] OR anti-TNF-alpha[Title/Abstract] OR TNF-alpha block*[Title/Abstract] OR TNF-alpha antagonist*[Title/Abstract] OR "Receptors, Interleukin/antagonists and inhibitors"[Mesh] OR interleukin inhibitor*[Title/Abstract] OR anti-interleukin[Title/Abstract] OR interleukin block*[Title/Abstract] OR interleukin antagonist*[Title/Abstract] OR "Janus Kinases/antagonists and inhibitors"[Mesh] OR janus kinase inhibitor*[Title/Abstract] OR anti-janus kinase[Title/Abstract] OR janus kinase block*[Title/Abstract] OR janus kinase antagonist*[Title/Abstract] OR JAK inhibitor*[Title/Abstract] OR anti-JAK[Title/Abstract] OR JAK block*[Title/Abstract] OR JAK antagonist*[Title/Abstract] OR "Antibodies, Monoclonal"[Mesh:NoExp] OR "Antibodies, Monoclonal, Humanized"[Mesh:NoExp] OR monoclonal antibod*[Title/Abstract] OR "Adalimumab"[Mesh] OR adalimumab[Text Word] OR Humira[Text Word] OR Amjevita[Text Word] OR Hyrimoz[Text Word] OR Cyltezo[Text Word]

OR "Certolizumab Pegol"[Mesh] OR Certolizumab[Text Word] OR Cimzia[Text Word] OR golimumab[Text Word] OR simponi[Text Word] OR CNTO148[Text Word] OR "CNTO 148"[Text Word] OR "Infliximab"[Mesh] OR infliximab[Text Word] OR Remicade[Text Word] OR Renflexis[Text Word] OR Inflectra[Text Word] OR Ixifi[Text Word] OR "Abatacept"[Mesh] OR Abatacept[Text Word] OR Orencia[Text Word] OR "Etanercept"[Mesh] OR Etanercept[Text Word] OR Enbrel[Text Word] OR Erelzi[Text Word] OR Secukinumab[Text Word] OR Cosentyx[Text Word] OR "AIN 457"[Text Word] OR AIN457[Text Word] OR Tofacitinib[Text Word] OR Xeljanz[Text Word] OR "CP 690550"[Text Word] OR CP690550[Text Word] OR Apremilast[Text Word] OR Otezla[Text Word] OR "CC 10004"[Text Word] OR CC10004[Text Word] OR Brodalumab[Text Word] OR Siliq[Text Word] OR "AMG 827"[Text Word] OR AMG827[Text Word] OR Ixekizumab[Text Word] OR Taltz[Text Word] OR "LY 2439821"[Text Word] OR LY2439821[Text Word] OR "Ustekinumab"[Mesh] OR Ustekinumab[Text Word] OR Stelara[Text Word] OR Upadacitinib[Text Word] OR ABT494[Text Word] OR "ABT 494"[Text Word] OR Guselkumab[Text Word] OR Tremfya[Text Word] OR "CNTO 1959"[Text Word] OR CNTO1959[Text Word] OR Tildrakizumab[Text Word] OR Ilumya[Text Word] OR "SCH 900222"[Text Word] OR SCH900222[Text Word] OR "MK 3222"[Text Word] OR MK3222[Text Word] OR Risankizumab[Text Word] OR Skyrizi[Text Word] OR "BI 655066"[Text Word] OR BI655066[Text Word] OR "ABBV 066"[Text Word] OR ABBV066[Text Word] OR Bimekizumab[Text Word] OR "UCB-4940"[Text Word] OR UCB4940[Text Word] OR "CDP-4940"[Text Word] OR CDP4940[Text Word] OR Remtolumab[Text Word] OR "ABT-122"[Text Word] OR ABT122[Text Word] OR "BMS-986165"[Text Word] OR BMS986165[Text Word] OR Deucravacitinib[Text Word] OR Mirikizumab[Text Word] OR "LY-3074828"[Text Word] OR LY3074828[Text Word]) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Psoriasis Terms AND Drug Terms

#3 #1 AND #2 AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

#4 (#3 NOT ("Animals"[Mesh] NOT "Humans"[Mesh])) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

#5 (#4 NOT ("Age Groups"[Mesh] NOT "Adult"[Mesh])) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Reviews Terms

#6 ("Systematic Review"[Publication Type] OR ((systematic[Title] OR structured[Title] OR evidence[Title] OR trials[Title]) AND (review[Title] OR overview[Title] OR look[Title] OR examination[Title] OR update*[Title] OR summary[Title] OR "Review"[Publication Type])) OR "0266-4623"[Journal] OR "1469-493X"[Journal] OR "1366-5278"[Journal] OR "1530-440X"[Journal] OR "Meta-Analysis"[Publication Type] OR "Network Meta-Analysis"[Mesh] OR meta-analys*[Text Word] OR meta analys*[Text Word] OR metaanalys*[Text Word] OR meta synth*[Text Word] OR meta-synth*[Text Word] OR metasynth*[Text Word] OR ("Review"[Publication Type] AND (medline[Text Word] OR medlars[Text Word] OR embase[Text Word] OR pubmed[Text Word] OR scisearch[Text Word] OR psychinfo[Text Word] OR psycinfo[Text Word] OR psychlit[Text Word] OR psyclit[Text Word] OR cinahl[Text Word] OR electronic database*[Text Word] OR bibliographic database*[Text Word] OR computerized

database*[Text Word] OR computerised database*[Text Word] OR online database*[Text Word] OR pooling[Text Word] OR pooled[Text Word] OR "mantel haenszel"[Text Word] OR peto[Text Word] OR dersimonian[Text Word] OR "der simonian"[Text Word] OR "fixed effect"[Text Word] OR hand search*[Text Word] OR manual search*[Text Word] OR manually search*[Text Word] OR "Retraction of Publication"[Publication Type] OR "Retracted Publication"[Publication Type])) OR systematic analys*[Title] OR systematic review[Title] OR meta-analys*[Title] OR meta-review[Title] OR systematic analys*[Other Term] OR systematic review[Title] OR meta-analys*[Other Term] OR meta-review[Other Term] OR systematic review*[Text Word] OR systematic overview*[Text Word] OR quantitative review*[Text Word] OR quantitative overview*[Text Word] OR methodological review*[Text Word] OR methodological overview*[Text Word] OR quantitative synthesis*[Text Word] OR integrative research review*[Text Word] OR "research integration"[Text Word] OR scoping review*[Title] OR scoping review*[Other Term] OR ((review[Title] OR review[Other Term] OR "Review"[Publication Type]) AND ("trials as topic"[Text Word] OR "studies as topic"[Text Word])) OR evidence review*[Text Word]) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

#7 (#6 NOT ("Case Reports"[Publication Type] OR "Letter"[Publication Type])) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Psoriasis Terms AND Drug Terms AND Reviews Terms

#8 #7 AND #5 AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

RCT Terms

#9 ("Randomized Controlled Trial"[Publication Type] OR random*[Text Word] OR placebo[Text Word]) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Psoriasis Terms AND Drug Terms AND RCT Terms

#10 #9 AND #5 AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Adverse Events Terms

#11 ("Antirheumatic Agents/adverse effects"[Mesh] OR "Antibodies, Monoclonal/adverse effects"[Mesh] OR "Biological Products/adverse effects"[Mesh:NoExp] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh:NoExp] OR "Long Term Adverse Effects"[Mesh] OR adverse effect*[Title/Abstract] OR adverse event*[Title/Abstract] OR adverse consequence*[Title/Abstract] OR adverse impact*[Title/Abstract] OR adverse outcome*[Title/Abstract] OR adverse reaction*[Title/Abstract] OR dangerous effect*[Title/Abstract] OR dangerous event*[Title/Abstract] OR dangerous consequence*[Title/Abstract] OR dangerous impact*[Title/Abstract] OR dangerous outcome*[Title/Abstract] OR dangerous reaction*[Title/Abstract] OR harmful effect*[Title/Abstract] OR harmful event*[Title/Abstract] OR harmful consequence*[Title/Abstract] OR harmful impact*[Title/Abstract] OR harmful outcome*[Title/Abstract] OR harmful reaction*[Title/Abstract] OR indirect effect*[Title/Abstract] OR indirect event*[Title/Abstract] OR indirect consequence*[Title/Abstract] OR indirect impact*[Title/Abstract] OR indirect

outcome*[Title/Abstract] OR indirect reaction*[Title/Abstract] OR injurious effect*[Title/Abstract] OR injurious event*[Title/Abstract] OR injurious consequence*[Title/Abstract] OR injurious impact*[Title/Abstract] OR injurious outcome*[Title/Abstract] OR injurious reaction*[Title/Abstract] OR secondary effect*[Title/Abstract] OR secondary event*[Title/Abstract] OR secondary consequence*[Title/Abstract] OR secondary impact*[Title/Abstract] OR secondary outcome*[Title/Abstract] OR secondary reaction*[Title/Abstract] OR side effect*[Title/Abstract] OR side event*[Title/Abstract] OR side consequence*[Title/Abstract] OR side impact*[Title/Abstract] OR side outcome*[Title/Abstract] OR side reaction*[Title/Abstract] OR undesirable effect*[Title/Abstract] OR undesirable event*[Title/Abstract] OR undesirable consequence*[Title/Abstract] OR undesirable impact*[Title/Abstract] OR undesirable outcome*[Title/Abstract] OR undesirable reaction*[Title/Abstract] OR "drug survival"[Title/Abstract] OR "drug retention"[Title/Abstract] OR "drug longevity"[Title/Abstract] OR "drug adherence"[Title/Abstract] OR harm[Title] OR safety[Title] OR complication*[Title] OR toxicity[Title] OR mortality[Title] OR infection*[Title] OR tuberculosis[Title] OR herpes[Title] OR malignan*[Title] OR cancer*[Title] OR "heart failure"[Title] OR heart disease*[Title] OR cardiovascular risk[Title] OR lung disease*[Title] OR gastrointestinal perforation*[Title] Filters: English

Psoriasis Terms AND Drug Terms AND Adverse Events Terms

#12 #11 AND #5 AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Total

#13 (#8 OR #10 OR #12) AND ("2019/05/01"[Date - Publication] : "3000"[Date - Publication]) Filters: English

Cochrane Library Search Strategy

Cochrane Library (Wiley) – May 1, 2019 to August 25, 2021Psoriasis Terms

#1 [mh Psoriasis] OR (psoriasis OR psoriatic NEXT arthr*):ti,ab,kw with Cochrane Library publication date from Dec 2020 to Dec 2021

Drug Terms

#2 ("Biological Products" OR "Antibodies, Monoclonal" OR "Antibodies, Monoclonal, Humanized"):kw OR [mh "Tumor Necrosis Factor-alpha"/AI] OR [mh "Receptors, Interleukin"/AI] OR [mh "Janus Kinases"/AI] OR (biologic NEXT therap* OR biologics OR "tumor necrosis factor alpha" NEXT inhibitor* OR "anti-tumor necrosis factor alpha" OR "tumor necrosis factor alpha" NEXT block* OR "tumor necrosis factor alpha" NEXT antagonist* OR "TNF-alpha" NEXT inhibitor* OR "anti-TNF-alpha" OR "TNF-alpha" NEXT block* OR "TNF-alpha" NEXT antagonist* OR interleukin NEXT inhibitor* OR "anti-interleukin" OR interleukin NEXT block* OR interleukin NEXT antagonist* OR "janus kinase" NEXT inhibitor* OR "anti-janus kinase" OR "janus kinase" NEXT block* OR "janus kinase" NEXT antagonist* OR JAK NEXT inhibitor* OR "anti-JAK" OR JAK NEXT block* OR JAK NEXT antagonist* OR monoclonal NEXT antibod*):ti,ab OR [mh "Adalimumab"] OR [mh "Certolizumab Pegol"] OR [mh "Infliximab"] OR [mh "Abatacept"] OR [mh

"Etanercept"] OR [mh "Ustekinumab"] OR (adalimumab OR Humira OR Amjevita OR Hyrimoz OR Cyltezo OR Certolizumab OR Cimzia OR golimumab OR simponi OR CNTO148 OR "CNTO 148" OR infliximab OR Remicade OR Renflexis OR Inflectra OR Ixifi OR Abatacept OR Orencia OR Etanercept OR Enbrel OR Erelzi OR Secukinumab OR Cosentyx OR "AIN 457" OR AIN457 OR Tofacitinib OR Xeljanz OR "CP 690550" OR CP690550 OR Apremilast OR Otezla OR "CC 10004" OR CC10004 OR Brodalumab OR Siliq OR "AMG 827" OR AMG827 OR Ixekizumab OR Taltz OR "LY 2439821" OR LY2439821 OR Ustekinumab OR Stelara OR Upadacitinib OR ABT494 OR "ABT 494" OR Guselkumab OR Tremfya OR "CNTO 1959" OR CNTO1959 OR Tildrakizumab OR Ilumya OR "SCH 900222" OR SCH900222 OR "MK 3222" OR MK3222 OR Risankizumab OR Skyrizi OR "BI 655066" OR BI655066 OR "ABBV 066" OR ABBV066 OR Bimekizumab OR "UCB-4940" OR UCB4940 OR "CDP-4940" OR CDP4940 OR Remtolumab OR "ABT-122" OR ABT122 OR "BMS-986165" OR BMS986165 OR Deucravacitinib OR Mirikizumab OR "LY-3074828" OR LY3074828):ti,ab,kw with Cochrane Library publication date from Dec 2020 to Dec 2021

Psoriasis Terms AND Drug Terms

#3 #1 AND #2 with Cochrane Library publication date from Dec 2020 to Dec 2021 440

#4 #3 NOT ([mh "Animals"] NOT [mh "Humans"]) with Cochrane Library publication date from Dec 2020 to Dec 2021

#5 #4 NOT ([mh "Age Groups"] NOT [mh "Adult"]) with Cochrane Library publication date from Dec 2020 to Dec 2021

Reviews Terms

#6 ("Systematic Review" OR "Meta-Analysis"):pt OR (((systematic OR structured OR evidence OR trials):ti AND ((review OR overview OR look OR examination OR update* OR summary):ti OR (Review):pt)) OR ("International journal of technology assessment in health care" OR "Cochrane database of systematic reviews" OR "Health technology assessment" OR "Evidence report/technology assessment Summary"):so OR [mh "Network Meta-Analysis"] OR (meta NEXT analys* OR metaanalys* OR meta NEXT synth* OR metasynth*):ti,ab,kw OR ((Review):pt AND ((medline OR medlars OR embase OR pubmed OR scisearch OR psychinfo OR psycinfo OR psychlit OR psyclit OR cinahl OR electronic NEXT database* OR bibliographic NEXT database* OR computerized NEXT database* OR computerized NEXT database* OR online NEXT database* OR pooling OR pooled OR "mantel haenszel" OR peto OR dersimonian OR "der simonian" OR "fixed effect" OR hand NEXT search* OR manual NEXT search* OR manually NEXT search*):ti,ab,kw OR ("Retraction of Publication" OR "Retracted Publication"):pt)) OR (systematic NEXT analys* OR "systematic review" OR meta NEXT analys* OR "meta-review" OR scoping NEXT review*):ti OR (systematic NEXT review* OR systematic NEXT overview* OR quantitative NEXT review* OR quantitative NEXT overview* OR methodological NEXT review* OR methodological NEXT overview* OR quantitative NEXT synthesis* OR "integrative research" NEXT review* OR "research integration" OR evidence NEXT review*):ti,ab,kw OR (((review):ti OR (Review):pt) AND ("trials as topic" OR "studies as topic"):ti,ab,kw)) with Cochrane Library publication date from Dec 2020 to Dec 2021

#7 #6 NOT ("Case Reports" OR "Letter"):pt with Cochrane Library publication date from Dec 2020 to Dec 2021

Psoriasis Terms AND Drug Terms AND Reviews Terms

#8 #7 AND #5 with Cochrane Library publication date from Dec 2020 to Dec 2021

RCT Terms

#9 ("Randomized Controlled Trial"):pt OR (random* OR placebo):ti,ab,kw with Cochrane Library publication date from Dec 2020 to Dec 2021

Psoriasis Terms AND Drug Terms AND RCT Terms

#10 #9 AND #5 with Cochrane Library publication date from Dec 2020 to Dec 2021

Adverse Events Terms

#11 [mh "Antirheumatic Agents"/AE] OR [mh "Antibodies, Monoclonal"/AE] OR ("Biological Products" NEXT "adverse effects"):kw OR ("Drug-Related Side Effects and Adverse Reactions"):kw OR [mh "Long Term Adverse Effects"] OR (adverse NEXT effect* OR adverse NEXT event* OR adverse NEXT consequence* OR adverse NEXT impact* OR adverse NEXT outcome* OR adverse NEXT reaction* OR dangerous NEXT effect* OR dangerous NEXT event* OR dangerous NEXT consequence* OR dangerous NEXT impact* OR dangerous NEXT outcome* OR dangerous NEXT reaction* OR harmful NEXT effect* OR harmful NEXT event* OR harmful NEXT consequence* OR harmful NEXT impact* OR harmful NEXT outcome* OR harmful NEXT reaction* OR indirect NEXT effect* OR indirect NEXT event* OR indirect NEXT consequence* OR indirect NEXT impact* OR indirect NEXT outcome* OR indirect NEXT reaction* OR injurious NEXT effect* OR injurious NEXT event* OR injurious NEXT consequence* OR injurious NEXT impact* OR injurious NEXT outcome* OR injurious NEXT reaction* OR secondary NEXT effect* OR secondary NEXT event* OR secondary NEXT consequence* OR secondary NEXT impact* OR secondary NEXT outcome* OR secondary NEXT reaction* OR side NEXT effect* OR side NEXT event* OR side NEXT consequence* OR side NEXT impact* OR side NEXT outcome* OR side NEXT reaction* OR undesirable NEXT effect* OR undesirable NEXT event* OR undesirable NEXT consequence* OR undesirable NEXT impact* OR undesirable NEXT outcome* OR undesirable NEXT reaction* OR "drug survival" OR "drug retention" OR "drug longevity" OR "drug adherence"):ti,ab OR (harm OR safety OR complication* OR toxicity OR mortality OR infection* OR tuberculosis OR herpes OR malignan* OR cancer* OR "heart failure" OR heart NEXT disease* OR "cardiovascular risk" OR lung NEXT disease* OR gastrointestinal NEXT perforation* OR "gastro-intestinal" NEXT perforation*):ti with Cochrane Library publication date from Dec 2020 to Dec 2021

Psoriasis Terms AND Drug Terms AND Adverse Events Terms

#12 #11 AND #5 with Cochrane Library publication date from Dec 2020 to Dec 2021

Total

#13 (#8 OR #10 OR #12) with Cochrane Library publication date from Dec 2020 to Dec 2021" in Cochrane Reviews

Ongoing Studies

We searched the following DERP sources for ongoing studies. Search terms were selected depending on the information source (see below):

ClinicalTrials.gov – May 1, 2019 through December 7, 2021

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | psoriasis OR psoriatic | adalimumab OR Humira OR Amjevita OR Hyrimoz OR Cyltezo OR Certolizumab OR Cimzia OR golimumab OR simponi OR CNTO148 OR "CNTO 148" OR infliximab OR Remicade OR Renflexis OR Inflectra OR Ixifi OR Abatacept OR Orencia OR Etanercept OR Enbrel OR Erelzi | Adult, Older Adult

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | psoriasis OR psoriatic | Secukinumab OR Cosentyx OR "AIN 457" OR AIN457 OR Tofacitinib OR Xeljanz OR "CP 690550" OR CP690550 OR Apremilast OR Otezla OR "CC 10004" OR CC10004 OR Brodalumab OR Siliq OR "AMG 827" OR AMG827 | Adult, Older Adult

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | psoriasis OR psoriatic | Ixekizumab OR Taltz OR "LY 2439821" OR LY2439821 OR Ustekinumab OR Stelara OR Upadacitinib OR ABT494 OR "ABT 494" OR Guselkumab OR Tremfya OR "CNTO 1959" OR CNTO1959 | Adult, Older Adult

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | psoriasis OR psoriatic | Tildrakizumab OR Ilumya OR "SCH 900222" OR SCH900222 OR "MK 3222" OR MK3222 OR Risankizumab OR Skyrizi OR "BI 655066" OR BI655066 OR "ABBV 066" OR ABBV066 | Adult, Older Adult

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | psoriasis OR psoriatic | Bimekizumab OR "UCB-4940" OR UCB4940 OR "CDP-4940" OR CDP4940 OR "BMS-986165" OR BMS986165 OR Deucravacitinib OR| Adult, Older Adult |

Inclusion Criteria

Population

- Adults with plaque psoriasis
- Adults with psoriatic arthritis

Interventions

- Targeted immune modulators (TIMs) and respective biosimilars that the US Food and Drug Administration (FDA) has approved for the treatment of plaque psoriasis or psoriatic arthritis, and select pipeline drugs likely to be approved soon

Comparators

- For FDA-approved drugs: another listed TIM intervention (head-to-head comparison)
- For pipeline drugs: any listed TIM, standard of care, placebo

Outcomes

- Health Outcomes
  - Quality of life
  - Functional capacity
  - Productivity, ability to sustain employment
  - Clinical improvement
  - Disease remission
  - Pain

    - Reduction in disease-related hospitalizations
    - Reduction in disease-specific mortality
    - Rebound/flare
    - Steroid withdrawal
- Harms
    - Overall adverse events (AEs)
    - Withdrawals due to AEs
    - Serious adverse events (SAEs)
    - Specific AEs (e.g., lymphoma, all malignancies, serious infectious diseases, herpes zoster, opportunistic infections, congestive heart failure)
    - Mortality

Study Designs

- Randomized controlled trials (RCTs) with ≥ 12-week study duration
- Retrospective and prospective cohort studies comparing an intervention type to another for outcomes on harms
    - > 12-week study duration
    - Minimum total sample size of 1,000
    - Reports adjusted statistical head-to-head comparisons

Exclusion Criteria

We excluded studies if they were not published in English. We also excluded conference abstracts and data reported in press releases.

Screening

Two experienced researchers independently screened all titles and abstracts of identified documents. In cases in which there was disagreement about eligibility, a third experienced researcher resolved the disagreement. This method was repeated for full-text review of documents that could not be excluded by title and abstract screening.

Data Abstraction

One experienced researcher abstracted and entered data from eligible studies in a standardized way using DistillerSR. A second experienced researcher reviewed all the data entered. We attempted to resolve discrepancies through discussion. When discussion did not resolve the issue, a third experienced researcher settled disagreements.

Participant Characteristics and Association With Outcomes

When discussing risk and protective factors or variables in statistical models in DERP research products, in almost all cases, we are referring to associations of participant characteristics with outcomes, and not causation of outcomes. This is important because participant characteristics, such as race and ethnicity, serve as proxy or surrogate measures for underlying etiological factors not measured or evaluated in analyses. Etiological factors that might cause differences in outcomes for subgroups of participants could include systemic racism or other forms of systemic discrimination, stress, poverty, housing instability, or epigenetics. For example, by describing any

differences in outcomes by race and ethnic groups, we are noting observed associations; these associations are not caused by biological determinants of being Black, White, or Hispanic.

Risk of Bias Assessment

Risk of Bias of Included Studies

We assessed the risk of bias (RoB) of the included RCTs and cohort studies using standard instruments developed and adapted by DERP that are modifications of instruments used by national and international standards for RoB.[8-12] One experienced researcher independently rated the RoB of included studies. A second experienced researcher reviewed each assessment. Disagreement was managed by discussion.

Randomized Controlled Trials

Low-RoB RCTs include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of patients to study groups; low dropout rates; and intention-to-treat analyses. Low-RoB RCTs also have low potential for bias from conflicts of interest and funding source(s). Moderate-RoB RCTs have incomplete information about methods that might mask important limitations or a meaningful conflict of interest. High-RoB RCTs have clear flaws that could introduce significant bias.

Cohort Studies

Low-RoB cohort studies include a sample that is representative of the source population, have low loss to follow-up, and measure and consider relevant confounding factors. Low-RoB cohort studies also list their funding source(s) and have a low potential of bias from conflicts of interest. Moderate-RoB cohort studies might not have measured all relevant confounding factors or adjusted for them in statistical analyses, have loss to follow-up that could bias findings, consist of a sample that is not representative of the source population, or have potential conflicts of interest that are not addressed. High-RoB cohort studies have a clear, high RoB that would affect findings.

Certainty-of-Evidence Assessment

Overall Certainty of Evidence

We assigned each outcome a summary judgment for the overall certainty of evidence (CoE) based on the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation Working Group (GRADE).[13,14] Two independent experienced researchers assigned ratings, with disagreements resolved through discussion. The GRADE system defines the overall quality of a body of evidence for an outcome in the following manner:

- **High:** Raters are very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect. Typical sets of studies are RCTs with few or no limitations, and the estimate of effect is likely stable.
- **Moderate:** Raters are moderately confident in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

- **Low:** Raters have little confidence in the estimate of the effect of the intervention on the outcome. The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.
- **Very low:** Raters have no confidence in the estimate of the effect of the intervention on the outcome. The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.
- **Not applicable:** Researchers did not identify any eligible articles.

Appendix B. Full Evidence Tables

Table B1. Evidence Table for RCTs of TIMs for Plaque Psoriasis or Psoriatic Arthritis (Study and Population Characteristics)

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Al Mutairi et al., 2020[23] Kuwait Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Eligible participants also had genital psoriasis defined by sPGA of genitalia ≥ 3 and were either intolerant or unresponsive to topical therapy for genital psoriasis. Eligible participants were candidates for phototherapy and/or systemic therapy and were ineffectively controlled by topical therapy. Participants were excluded if they had previous history of treatment with IL-17 inhibitors, had any medical condition that might interfere with interpretation of study results, had psoriasis other than chronic plaque psoriasis, and had a previous history of any malignancy within the last 5 years.	Median (IQR) age in years 41 (18 to 64) N (%) female Ixekizumab: 7 (25) Secukinumab: 8 (31) NR	Mean (SD) duration of psoriasis in years • Ixekizumab: 17.3 (14.2) • Secukinumab: 18.7 (12.2) Mean (SD) duration of genital psoriasis • Ixekizumab: 8.2 (17.4) • Secukinumab: 8.4 (11.3) Mean (SD) PASI • Ixekizumab: 39.0 (12.6) • Secukinumab: 38.6 (14.3)	Not funded
Araujo et al., 2019[43] Germany ECLIPSA EudraCT 2017-003799-29 High	Adults (> 18 years of age) with a diagnosis of PsA according to CASPAR criteria, presence of active enthesitis defined as 1 painful entheses using the SPARCC EI, and methotrexate treatment failure for at least 3 months. Participants who had received or were receiving biological DMARD therapy were excluded from the study.	Mean age (SD) in years • Ustekinumab: 62 (18) • TNF inhibitor: 58 (21) 19 (40.2%) female Race/ethnicity: NR	Duration of PsA, Mean (SD) in years • Ustekinumab: 2 (6.0) • TNF inhibitor: 3 (4.8) N (%) with concomitant treatment Glucocorticoids • Ustekinumab: 0 (0) • TNF inhibitor: 1 (4.2)	Deutsche Forschungs-gemein-schaft; Bundes-ministerium fur Bildung und Forschung

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
	Glucocorticoids of less than 5 mg of prednisolone/day were allowed during the study.		Methotrexate • Ustekinumab: 19* (82) • TNF inhibitor: 24 (100)	(government agencies)
Atteno et al., 2010[50] Italy High	Adults (≥ 18 years of age) with psoriatic arthritis and inadequate response to previous DMARDs therapy. Participants were excluded if they had previous used anti-TNF-α inhibitors, DMARDs (other than sulfasalazine, methotrexate, azathioprine, or leflunomide) within 4 weeks of enrollment, more than 10 mg prednisone daily, or had changed dosage of NSAIDs or prednisone within 2 weeks of enrollment.	Mean (SD) age in years: 48.5 (12.5) 60 (60%) female Race/ethnicity: NR	Median (IQR) PASI: 19 (18.2) Median (IQR) HAQ: 1.2 (0.4) Median (range) duration of disease in months: 80 (20 to 140)	NR
Bachelez et. al., 2015[62] Valenzuela et al., 2016[63] Multiple countries (not US or Canada) OPT NCT01241951 Moderate	18 years of age or older diagnosed with chronic (≥ 12 months) stable plaque psoriasis; candidate for systemic therapy or phototherapy; PASI score ≥ 12; IGA of moderate or severe psoriasis that involved at least 10% of BSA; failed to respond to, had a contraindication to, or were intolerant to at least 1 conventional systemic therapy (including ultraviolet therapy).	Age: NR Gender: NR Race/ethnicity: NR (most White)	NR	Pfizer
Bagel et al., 2018[39] Bagel et al., 2021[77] US, Canada, Czech, Guatemala, Hungary, Iceland,	Adults with moderate-to-severe chronic plaque psoriasis defined by PASI ≥ 12, static 5-point IGA 2011 modified version score ≥ 3, and BSA involvement ≥ 10%. Eligible	Mean age (SD) in years • Secukinumab: 45.4 (14.1) • Ustekinumab: 45.3 (14.2)	PASI, Mean (SD) • Secukinumab: 20.8 (9.0) • Ustekinumab: 21.3 (9.2) Mean time since first diagnosis of plaque-type	Novartis Pharma AG

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Korea, Malaysia, Poland, Slovakia, Vietnam CLARITY NCT02826603 Moderate	participants were also inadequately controlled by topical treatments, phototherapy, and/or previous systemic therapy.	370 (33.6%) female 278 (25.2%) non-White population	psoriasis, mean (SD) in years • Secukinumab: 16.8 (11.9) • Ustekinumab: 17.3 (13.3)	
Blauvelt et al., 2020[17] Blauvelt et al., 2021[36] US and Canada IXORA-R NCT03573323 Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Eligible participants were also candidates for systemic therapy and/or phototherapy. Participants were excluded if they had nonplaque psoriasis, history of drug-induced psoriasis, used a tanning booth 4 weeks before baseline, used any biological agent within specified periods prior to baseline, used any IL-23p19 antagonists, or had any condition as addressed in the local labeling for guselkumab.. Prior use of an IL-17 antagonist was allowed if the patient had not failed to respond to the therapy.	Mean (SD) age in years 49.0 (14.4) 375 (37%) Female 870 (84.7%) White	Mean (SD) duration of psoriasis in years • Ixekizumab: 17.5 (13.8) • Guselkumab: 16.3 (13.8) Mean (SD) PASI • Ixekizumab: 19.5 (7.9) • Guselkumab: 19.3 (7.1)	Eli Lilly and Company
Blauvelt et al., 2017[69] Papp et al., 2018[70] US, Australia, Canada, Germany, Hungary, Republic of Korea, Poland, Russian Federation, Spain, Taiwan	Adults with moderate-to-severe psoriasis for ≥ 6 months, ≥ 10% BSA, ≥ 12 PASI, ≥ 3 IGA. Participants were included if they were candidates for phototherapy. Participants were excluded if they had a history of an	Mean (SD) age in years • Adalimumab: 42.9 (12.6) • Guselkumab: 43.9 (12.7) N (%) female • Adalimumab: 85 (25.4) • Guselkumab: 89 (27.1) N (%) White	Mean (SD) duration of psoriasis in years • Adalimumab: 17.0 (11.3) • Guselkumab: 17.9 (12.3) Mean (SD) PASI • Adalimumab: 22.4 (9.0) • Guselkumab: 22.1 (9.5)	Janssen Research & Development

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
VOYAGE-1 NCT02207231 Moderate	uncontrolled medical condition or malignancy, except nonmelanoma skin cancer within 5 years. Patient were excluded if they had a history of TB, had received guselkumab or adalimumab or other anti-TNF-α therapy (within 3 months), other treatment targeting IL 12/23, IL-17 or IL-23 (6 months), or any systemic immunosuppressants or phototherapy (4 weeks).	• Adalimumab: 277 (82.9) • Guselkumab: 262 (79.6) N (%) Asian • Adalimumab: 47 (14.1) • Guselkumab: 51 (15.5) N (%) Black • Adalimumab: 8 (2.4) • Guselkumab: 6 (1.8)		
Blauvelt et al., 2017[41] Blauvelt et al. 2016[42] Thaci et al., 2015[40] Worldwide CLEAR NCT02074982 Moderate	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and ≥ 10% BSA, PASI of 12 or greater, IGA 2011 modified version 3 (moderate) or 4 (severe) and inadequate response to topical treatment, and/or phototherapy, and/or previous systemic therapy (conventional or biologic).	Age: mean age 45 Gender: 68 to 74% male Race/ethnicity: 85% to 89% White	NR	Novartis
De Vries et al., 2017[64] The Netherlands PIECE Dutch Trials Registry 1559 High	Adults with moderate-to-severe chronic plaque psoriasis (with PASI ≥ 10, and/or BSA ≥ 10 and/or PASI ≥ 8 plus Skindex-29 ≥ 35).	Age: mean age in the 2 groups ranged from 42 to 46 years of age Gender: 28 to 44% females Race/ethnicity: NR	Participants must have failed or were contraindicated for and/or intolerant to UV therapy, and methotrexate or ciclosporin Washout period was 2 weeks for topical and UV therapy and 4 weeks for systemic therapies	The Netherlands Organization for Scientific Research-Medical Sciences
Glatt et al., 2017[53]	Adults (ages 18 to 70) with plaque-type psoriasis for at least 6 months involving	Mean (SD) age in years • Placebo: 38.2 (13.3)	Median (range) PASI score • Placebo 3.0 (1.8 to 6.1)	UCB Pharma

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
UK NCT02529956 Moderate	more than 5% of BSA (excluding the scalp) and at least 2 psoriatic lesions with at least 1 plaque in a suitable biopsy site. Participants were excluded if they were using systemic nonbiological psoriasis therapy or phototherapy (within 4 weeks prior to screening), and treatment with biological agents (within 12 months prior to screening).	• Bimekizumab: 39.5 (10.4) N (%) female • Placebo: 1 (7.3) • Bimekizumab: 9 (23.1) N (%) Asian • Placebo: 0 (0) • Bimekizumab: 1 (2.6) N (%) other/mixed • Placebo: 0 (0) • Bimekizumab: 1 (2.6) N (%) Caucasian • Placebo: 13 (100) • Bimekizumab: 37 (94.9) N (%) Hispanic or Latino • Placebo: 0 (0) • Bimekizumab: 0 (0)	• Bimekizumab: 3.5 (0.8 to 6.7)	
Gordon et al., 2021[22] Australia, Canada, Germany, Hungary, Poland, Russia, South Korea, UK, US BE READY NCT03410992 Moderate	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Eligible participants were candidates for systemic psoriasis therapy or phototherapy, or both. Eligible participants could have a co-diagnosis of psoriatic arthritis and could take stable doses of NSAIDs or analgesics as needed. Participants were excluded if they had previously received at least 1 dose of bimekizumab; had experienced primary failure to any anti-IL-17 biologic or more than 1 biologic other than IL-17; had a form of psoriasis	Mean (SD) age in years • 44.3 (12.9) • 122 (28%) Female • 403 (93%) White • 32 (7%) Other	Mean (SD) duration of psoriasis in years • 19.5 (13.2) Mean (SD) PASI • 20.3 (7.6) N (%) previous biologic therapy 192 (44)	UCB Pharma

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
	other than chronic plaque-type psoriasis; had a current, or history of, opportunistic, recurrent, or chronic infection; had active Crohn's disease or ulcerative colitis; or had severe major depression or presence of active suicidal ideation or suicidal behavior.			
Gordon et al., 2018[67] Augustin et al., 2020[78] Australia, Austria, Belgium, Canada, Czech Republic, France, Germany, Japan, Mexico, Poland, Portugal, South Korea, Spain, and US UltIMMa-1, UltIMMa-2 NCT02684357, NCT02684370 Moderate	Adult with moderate-to-severe plaque psoriasis ≥ 6 months and involving 10% BSA, PASI ≥ 12, PGA ≥ 3. Participants were included if they were candidates for systemic therapy or phototherapy and eligible for treatment with ustekinumab.	Mean (SD) age in years • Risankizumab: 48.3 (13.4) • Ustekinumab: 46.5 (13.4) N (%) female • Risankizumab: 92 (30) • Ustekinumab: 30 (30) N (%) White • Risankizumab: 200 (66) • Ustekinumab: 74 (74) N (%) Black or African American • Risankizumab: 10 (3) • Ustekinumab: 1 (1) N (%) Asian • Risankizumab: 86 (28) • Ustekinumab: 22 (22) N (%) other • Risankizumab: 8 (3) • Ustekinumab:3 (3)	Mean (SD) PASI • Risankizumab: 20.6 (7.7) • Ustekinumab: 20.1 (6.8)	AbbVie and Boehringer Ingelheim
Gordon et al., 2015[74] US, Belgium, Germany, Poland, and Canada	Adults age 18 and older with moderate-to-severe psoriasis with at least 10% BSA involvement, ≥ 3 PGA score; ≥ 12 PASI; participants were	Median age in years • Adalimumab: 50.0 • Guselkumab: 44.0 N (%) female • Adalimumab: 13 (30)	Mean (SD) duration of psoriasis in years • Adalimumab: 19.3 (12.8) • Guselkumab: 18.5 (12.2) Mean (SD) PASI score	Janssen Research and Development

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
X-PLORE NCT01483599 Moderate	excluded if they had previously been exposed to adalimumab or guselkumab.	• Guselkumab: 59 (28) N (%) White • Adalimumab: 39 (91) • Guselkumab: 189 (91)	• Adalimumab: 20.2 (7.6) • Guselkumab: 20.9 (8.1)	
Griffiths et al., 2010[51] Worldwide NCT0045484 Moderate	Adults age 18 and older with moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA, PGA score of 3 or more, PASI score of 12 or more.	Mean age in years • Etanercept: 45.7 • Ustekinumab 45 mg: 45.1 • Ustekinumab 90 mg: 44.8 N (%) female • Etanercept: 101 (29) • Ustekinumab 45 mg: 76* (36) • Ustekinumab 90 mg: 113 (33) N (%) White • Etanercept: 316 (91) • Ustekinumab 45 mg: 193 (92) • Ustekinumab 90 mg: 309 (89)	Mean (SD) duration of psoriasis in years • Etanercept: 18.8 (12.1) • Ustekinumab 45 mg: 18.9 (11.8) • Ustekinumab 90 mg: 18.7 (11.8) Mean (SD) PASI score • Etanercept: 18.6 (6.2) • Ustekinumab 45 mg: 20.5 (9.2) • Ustekinumab 90 mg: 19.9 (8.4)	Centocor Research and Development
Griffiths et al., 2015[68] Multiple countries including UK, Germany, US, Netherlands, France UNCOVER-2, UNCOVER-3 NCT01597245, NCT01646177 Moderate	Adults with at least moderate-to-severe plaque psoriasis ≥ 6 months' duration and involving ≥ 10% BSA, PGA score of 3 or more, PASI score of 12 or more.	Mean age in the 2 trials ranged from 45 to 46 years of age Gender: 63 to 71% males Race/ethnicity: White ranged from 89 to 94%	NR	Eli Lilly and Company

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Langley et al., 2014[45] Worldwide FIXTURE NCT01358578 Moderate	18 years of age or older with moderate-to-severe plaque psoriasis that had been diagnosed at least 6 months before randomization and that was poorly controlled with topical treatments, phototherapy, systemic therapy, or a combination. Score of 12 or higher on PASI; score of 3 or 4 on the modified IGA, and involvement of 10% or more of the BSA. Psoriasis other than chronic plaque type (e.g., drug-induced) were excluded. Medications that might confound efficacy were not allowed.	Mean age NR Gender: 71% Race/ethnicity: 67% White	14 to 27% concurrent psoriatic arthritis, BSA affected around 33%, rates of previous TNF inhibitor or biologic 4% to 30%	Novartis
Lebwohl et al., 2018[15] North America and Europe CIMPACT NCT02346240 Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Eligible participants were also candidates for systemic psoriasis therapy, phototherapy, or photochemotherapy. Participants were excluded if they had nonplaque psoriasis, history of recurrent infections or high risk for infection, malignancy, congestive heart failure, history of prior treatment with certolizumab pegol or etanercept, or failure of more than 2 biologic agents.	Mean (SD) age in years • Certolizumab pegol 200 mg: 46.7 (13.5) • Certolizumab pegol 400 mg: 45.4 (12.4) • Etanercept: 44.6 (14.1) N (%) female • Certolizumab pegol 200 mg: 52 (31.5) • Certolizumab pegol 400 mg: 60 (35.9) • Etanercept: 43 (25.3) N (%) White • Certolizumab pegol 200 mg: 158 (95.8) • Certolizumab pegol 400 mg: 162 (97.0) • Etanercept: 163 (95.9)	Mean (SD) duration of psoriasis in years • Certolizumab pegol 200 mg: 19.5 (13.2) • Certolizumab pegol 400 mg: 17.8 (11.5) • Etanercept: 17.4 (12.0) Mean (SD) PASI • Certolizumab pegol 200 mg: 21.4 (8.8) • Certolizumab pegol 400 mg: 20.8 (7.7) Etanercept: 21.0 (8.2)	Dermira Inc and UCB Inc

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Lebwohl et al., 2015[37] Hsu et al., 2020[76] Lambert et al., 2021[82] Warren et al., 2021[81] 142 sites worldwide AMAGINE-2, AMAGINE-3 NCT01708603, NCT01708629 Moderate	Adults 18 to 75 years of age with stable moderate-to-severe plaque psoriasis ≥ 6 months' duration, ≥ 10% BSA, PASI of 12 or greater, PGA score of 3 or higher.	Age: mean age 45 Gender: 68 to 69% male Race/ethnicity: 90 to 91% White	NR	Amgen
McInnes et al., 2021[26] 45 countries, including US SELECT-PsA 1 NCT03104400 Moderate	Adults age 18 and older with psoriatic arthritis who fulfilled the Classification Criteria for Psoriatic Arthritis. Eligible participants also had historical or current plaque psoriasis. Eligible participants had at least 3 tender joints (of 68 tested), the presence of 1 or more erosions on the hands or feet on radiography or a high-sensitivity C-reactive protein level, and an inadequate response or unacceptable side effects with at least 1 nonbiologic DMARD. Participants were excluded if they had previous exposure to biologic therapies or JAK inhibitors.	Mean (SD) age in years • Upadacitinib 15 mg: 51.6 (12.2) • Upadacitinib 30 mg: 49.9 (12.4) • Adalimumab: 51.4 (12.0) N (%) female • Upadacitinib 15 mg: 238 (55.5) • Upadacitinib 30 mg: 236 (55.8) • Adalimumab: 222 (51.7) N (%) White • Upadacitinib 15 mg: 386 (90.0) • Upadacitinib 30 mg: 377 (89.1) • Adalimumab: 375 (87.4)	Mean (SD) duration of psoriatic arthritis in years • Upadacitinib 15 mg: 6.2 (7.4) • Upadacitinib 30 mg: 5.9 (6.4) • Adalimumab: 5.9 (7.1) Mean (SD) PASI • Upadacitinib 15 mg: 9.8 (10.0) • Upadacitinib 30 mg: 9.5 (8.8) • Adalimumab: 9.4 (8.5)	AbbVie
McInnes et al., 2020[16] Gottlieb et al., 2021[35] 26 countries	Adults age 18 and older who were naïve to treatment with biologics with active psoriatic arthritis defined as ≥ 3 swollen joints and ≥ 3 tender joints and	Mean (SD) age in years: • 49.0 (12.4) 416 (49%) Female 793 (93%) White	Mean time (SD) since first diagnosis of psoriatic arthritis, in years: 5.4 (7.5)	Novartis

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
EXCEED NCT02745080 Moderate	with active plaque psoriasis defined as having at least 1 plaque of at least 2 cm diameter or nail changes consistent with psoriasis. Eligible participants also had an inadequate response to previous DMARDs therapy and previous NSAIDs therapy for at least 4 weeks before randomization. Eligible participants who were on concomitant corticosteroids were required to be on a stable dose of 10 mg/day or less of prednisone. Participants were excluded if pregnant, showed evidence of ongoing infection or malignancy, had previous exposure to any biologicals or opioids, had ongoing use of oral or topical retinoids, photochemotherapy, phototherapy, or topical skin treatment. Washout period of 4 to 8 weeks for csDMARDs required.	36 (4%) Asian 24 (3%) Other	PtGA (0 to 100): 62.9 (20.2) Baseline PASI Score, Mean (SD): 10.3 (8.6) Participants with psoriasis (BSA ≥3%): 417 (49%) Participants with psoriasis (BSA >10% or PASI ≥10): 211 (25%)	
Mease et al., 2020[18] Smolen et al., 2020[33] Smolen et al., 2020[34] Multicountry SPIRIT-H2H NCT03151551 Moderate	Adults with psoriatic arthritis ≥ 6 months' duration defined by the Classification for Psoriatic Arthritis criteria of having at least 3/66 swollen and 3/68 tender joints. Eligible participants also had active plaque psoriasis with BSA involvement ≥ 3%. Eligible participants had previous inadequate response to ≥ 1 csDMARD and had not previously received bDMARD or Janus kinase inhibitor therapy. Eligible participants on csDMARDs at screening were allowed	Mean (SD) age in years • Ixekizumab: 47.5 (12.0) • Adalimumab: 48.3 (12.3) N (%) female • Ixekizumab: 121 (43) • Adalimumab: 133 (47) N (%) White • Ixekizumab: 222 (78) • Adalimumab: 211 (75) N (%) Asian • Ixekizumab: 29 (10) • Adalimumab: 33 (12)	Mean (SD) duration of symptoms since PsA diagnosis in years • Ixekizumab: 6.6 (7.4) • Adalimumab: 5.9 (6.4) Mean (SD) duration of symptoms since psoriasis diagnosis in years • Ixekizumab: 16.1 (13.1) • Adalimumab: 14.7 (12.6) Mean (SD) PASI • Ixekizumab: 7.9 (8.7) • Adalimumab: 7.7 (7.3)	Eli Lilly and Company

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
	to continue a stable dose of csDMARD therapy.		N (%) concomitant csDMARD use • Ixekizumab: 193 (68) • Adalimumab: 199 (70) N (%) concomitant methotrexate use • Ixekizumab: 167 (59) • Adalimumab: 169 (60)	
Mease et al., 2017[60] Strand et al., 2019[61] 126 centers worldwide OPAL Broaden NCT01877668 Moderate	Adults with active psoriatic arthritis of at least 6 months, TNF-inhibitor-naïve with an inadequate response to at least 1 DMARD.	Age: mean age in the 3 active groups ranged from 47 to 49 years of age Gender: 47% to 60% were females Race/ethnicity: 93% to 98% White	88% of tofacitinib 10 mg group had concomitant use of methotrexate, 85% of tofacitinib 5 mg group, and 75% of the adalimumab group	Pfizer
Mease et al., 2017[66] SPIRIT-P1 NCT01695239 Moderate	Adults with active psoriatic arthritis of at least 6 months, biologic therapy-naïve	Age: Mean age in the 3 active groups ranged from 49 to 50 years of age Gender: 42 to 51% were males Race/ethnicity: 93 to 95% White	Methotrexate use ranged from 53 to 56%	Eli Lilly

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Papp et al., 2018[54] US, Japan, Poland, Canada, Germany, Latvia, Mexico, and Australia NCT02931838 Moderate	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration; BMI between 18 and 40; eligible for phototherapy or systemic therapy; BSA ≥ 10%; PASI ≥ 12; PGA ≥ 3.	Mean (SD) age in years • Placebo: 46 (12) • Deucravacitinib: 45 (13) N (%) female • Placebo: 8* (18)* • Deucravacitinib: 73* (27)* N (%) White • Placebo: 40 (89) • Deucravacitinib: 225 (84) N (%) Asian • Placebo: 5 (11) • Deucravacitinib: 36 (13) N (%) other • Placebo: 0 (0) • Deucravacitinib: 6 (2)	Median (range) duration of disease in years • Placebo: 18 (2 to 48) • Deucra-vacitinib: 15 (1 to 61) Mean (SD) PASI score • Placebo: 19 (6) • Deucra-vacitinib: 18 (6)	Bristol-Myers Squibb
Papp et al., 2018[38] Canada, Czech Republic, Hungary, Japan, Poland, and US BE ABLE 1 NCT02905006 Moderate	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration, involving ≥ 10% BSA., IGA score of ≥ 3 on a 5-point scale, and who were candidates for systemic psoriasis therapy or phototherapy. Participants were excluded if they had prior treatment with an anti-IL-17 therapy or prior exposure to > 1 other biologic therapy for psoriasis or psoriatic arthritis, a significant uncontrolled neuropsychiatric disorder, history of a suicide attempt, or suicide ideation within 6 months.	Mean (SD) age in years: 44.3 (13.7) 87 (34.8%) female 223 (89.2%) White	Disease duration, years, median (range), 15.0 (0 to 58.7) PASI, mean (SD), 19.1 (6.5) N (%) other characteristics • Prior systemic therapy 177 (70.8) • Prior biologic therapy 58 (23.2) • Prior nonbiologic systemic therapy 90 (36.0) • Prior systemic phototherapy 122 (48.8)	UCB Pharma

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Papp et al., 2017[52] 32 sites across North America and Europe NCT02054481 Moderate	Adults 18 to 75 years of age with stable moderate-to-severe chronic plaque psoriasis > 6 months' duration, with or without psoriatic arthritis, involving ≥ 10% BSA, PASI score of 12 or higher PGA score of 3 or higher, biologic-naïve.	Age: mean age 46 ± 14 Gender: 66% male Race/ethnicity: 91% White	NR	Boehringer Ingelheim
Reich et al., 2017[73] Reich et al., 2019[71] Gordon et al., 2018[72] US, Australia, Canada, Czechia, Germany, Hungary, Republic of Korea, Poland, Russia, Spain, Taiwan VOYAGE-2 NCT02207244 Moderate	Adults (aged ≥ 18 years) with moderate-to-severe plaque psoriasis (as per IGA score ≥ 3, PASI score ≥ 12, BSA ≥ 10%) for at least 6 months and were candidates for systemic therapy or phototherapy. Participants were ineligible if they had a history or current signs of a severe, progressive, or uncontrolled medical condition or had current or history of malignancy, except nonmelanoma skin cancer, within 5 years. Participants could not participate if they received guselkumab or adalimumab previously; other anti-TNF-α therapy (within 3 months); other treatment targeting IL-12/23, IL-17, or IL-23 (6 months); or any systemic immunosuppressants (e.g., methotrexate) or phototherapy (4 weeks).	Mean age (SD) in years • Adalimumab: 43.2 (11.9) • Guselkumab: 43.7 (12.2) 225 (30.2%) female among guselkumab and adalimumab groups 11 (1.48%) African American 109 (14.7%) Asian among guselkumab and adalimumab groups	Duration of psoriasis, Mean (SD) in years • Adalimumab: 17.6 (11.7) • Guselkumab: 17.9 (12.0) PASI score, 0 to 72, Mean (SD) • Adalimumab: 21.7 (9.0) • Guselkumab: 21.9 (8.8) Prior biologic agents, N (%) 50 (20.2%)	Janssen Research & Development
Reich et al., 2019[44] Blauvelt et al., 2021[80] Australia, Canada, Czech Republic, France, Germany, Hungary, Poland, Spain, US	Participants with moderate-to-severe psoriasis over the age of 18; PASI ≥ 12; IGA ≥ 3; BSA ≥ 10%, for ≥ 6 months who were candidates for phototherapy or systemic therapy. Participants were	Mean (SD) age in years • Overall: 45.8 (13.6) • Guselkumab: 46.3 (13.7) • Secukinumab: 45.3 (13.6) N (%) female	Mean (SD) PASI 20.0 (7.5) Duration of psoriasis in years 18.4 (12.4)	Janssen Research & Development

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
ECLIPSE NCT03090100 Moderate	excluded if they had an uncontrolled medical condition, current or history of malignancy (except nonmelanoma skin cancer), inflammatory bowel disease, had previously taken guselkumab and secukinumab or any therapeutic agent directly targeted to IL12/23p40, IL-17 A, IL-17R, or IL-23 within 6 months prior to enrollment, or any systemic immunosuppressant or phototherapy within 4 weeks before enrollment.	• Overall: 341 (33) • Guselkumab: 169 (32) • Secukinumab: 172 (33) N (%) White: • Overall: 979 (93) • Guselkumab: 499 (93) • Secukinumab: 480 (93) N (%) Asian: • Overall: 30 (3) • Guselkumab: 18 (3) • Secukinumab: 12 (2) N (%) Black or African American: • Overall: 16 (2) • Guselkumab: 5 (1) • Secukinumab: 11 (2) N (%) other: • Overall: 23 (2) • Guselkumab: 12 (2) • Secukinumab: 11 (2)		
Reich et al., 2019[46] Canada, Czech Republic, Germany, Finland, France, Mexico, Poland, Portugal, Sweden, Taiwan, US IMMvent NCT02694523 Moderate	Adults (aged ≥18 years) with moderate-to-severe chronic plaque psoriasis ≥ 6 months, involving ≥ 10% BSA, with a PASI of 12 or higher, and a static PGA score of 3 or higher. Participants were required to be candidates for systemic therapy or phototherapy and eligible for adalimumab treatment in accordance with local approved labeling.	Mean age (SD) in years • Risankizumab: 45.3 (13.8) • Adalimumab: 47.0 (13.1) 183 (30.2%) female 17 (2.81%) Black or African American 76 (12.6%) Asian 508 (83.9%) White 4 (0.1%) Other	PASI, Mean (SD) • Risankizumab: 20.0 (7.5) • Adalimumab: 19.7 (7.5) Any previous biologic treatment, N (%) • Risankizumab: 118 (39%) • Adalimumab: 111 (37%) Previous non-TNF-α treatment, N (%) • Risankizumab: 95 (32%) • Adalimumab: 83 (27%)	AbbVie and Boehringer Ingelheim

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
Reich et al., 2017[65] Reich et al., 2020[75] Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Hungary, Italy, Israel, Netherlands, Poland, and US reSurface-2 NCT01729754 Moderate	Adults with moderate-to-severe plaque psoriasis involving ≥ 10% BSA., ≥ 3 PGA, ≥ 12 PASI, candidates for phototherapy or systemic therapy, women could not be pregnant and those of childbearing age had to practice abstinence or use contraception. Participants were excluded if they had active or latent tuberculosis, infection requiring antibiotic treatment with 2 weeks of screening, severe infection requiring hospital admission of intravenous antibiotics within 8 weeks of study, live viral or bacterial vaccination within 4 weeks of study, HIV, hepatitis B, hepatitis C, previous malignancy, hospitalization for acute cardiovascular event, illness, or surgery within 6 months of trials, uncontrolled hypertension, uncontrolled diabetes, or previous use of tildrakizumab or etanercept.	Mean (SD) in years • Placebo: 46.4 (12.2) • Etanercept: 45.8 (14.0) • Tildrakizumab 100 mg: 44.6 (13.6) • Tildrakizumab 200 mg: 44.6 (13.6) N (%) female • Placebo: 89* (28)* • Etanercept: 87* (28)* • Tildrakizumab 100 mg: 91* (29)* • Tildrakizumab 200 mg: 44* (28)* N (%) White • Placebo: 144 (92) • Etanercept: 289 (92) • Tildrakizumab 100 mg: 279 (91) • Tildrakizumab 200 mg: 284 (90) N (%) Asian • Placebo: 3 (2) • Etanercept: 10 (3) • Tildrakizumab 100 mg: 9 (3) • Tildrakizumab 200 mg: 14 (4) N (%) other • Placebo: 9 (6) • Etanercept: 14 (4) • Tildrakizumab 100 mg: 19 (6)	Mean (SD) % BSA • Placebo: 31.3 (14.8) • Etanercept: 31.6 (16.6) • Tildrakizumab 100 mg: 34.2 (18.5) • Tildrakizumab 200 mg: 31.8 (17.2) Mean (SD) PASI • Placebo: 20.0 (7.6) • Etanercept: 20.2 (7.4) • Tildrakizumab 100 mg: 20.5 (7.6) • Tildrakizumab 200 mg: 19.8 (7.5) N (%) previously treated with biologics • Placebo: 20 (13) • Etanercept: 37 (12) • Tildrakizumab 100 mg: 39 (13) • Tildrakizumab 200 mg: 38 (12	Merck & Co

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
		• Tildrakizumab 200 mg: 16 (5)		
Reich et al., 2017[47] Paul et al., 2018[48] Wasel et al., 2020[79] Puig et al., 2020[83] IXORA-S NCT02561806 Moderate	Adults with moderate-to-severe plaque psoriasis ≥ 6 months' duration and PASI ≥ 10, PASI score ≥ 10; previously failed or had a contraindication or intolerability to at least 1 systemic therapy (including ciclosporin, methotrexate and phototherapy).	Age: mean age for both groups 43 to 44 Gender: 66 to 68% male Race/ethnicity: 93 to 96% White	NR	Eli Lilly and Company
Reich et al., 2017[49] Multiple Countries including Germany, Canada, US, UK LIBERATE NCT01690299 Moderate	Adults with moderate-to-severe plaque psoriasis for ≥ 12 months (BSA ≥ 10%, PASI ≥ 12, PGA ≥ 3) and inadequate response, intolerance or contraindication to ≥ 1 conventional systemic agent for treatment of psoriasis, no prior exposure to a biologic therapy.	Age: mean age in the 2 groups ranged from 46 to 47 years of age Gender: 59% to 70% males Race/ethnicity: 90% to 95% White	NR	Celgene Corporation
Reich et al., 2021[21] Australia, Belgium, Canada, Germany, Hungary, Italy, Japan, Poland, Russia, UK, US BE VIVID NCT03370133 Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, IGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Eligible participants were also candidates for systemic psoriasis therapy, phototherapy, or both. Participants were excluded if they had previously received bimekizumab, ustekinumab, or both; had primary failure to any anti-IL-17 biologic; had psoriasis other than chronic plaque	Mean (SD) age in years 46.1 (13.9) 161 (28%) Female N (%) White: 420 (74) N (%) American Indian or Alaskan native: 2 (<1) N (%) Asian: 127 (22) N (%) Black: 12 (2) N (%) Native Hawaiian or other Pacific Islander: 0 (0) N (%) other or mixed race: 6 (1)	Mean (SD) duration of psoriasis in years: 17.1 (12.0) Mean (SD) PASI: 21.5 (8.3)	UCB Pharma

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
	type; had a history of, opportunistic, recurrent, or chronic infection; or had active Crohn's disease or ulcerative colitis.			
Reich et al., 2021[24] Multicountry BE RADIANT NCT03536884 Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Participants were excluded if they had previous exposure to bimekizumab or secukinumab and if had no response within 12 weeks to an anti-IL17 biologic agent or to more than 1 biologic agent of any other class.	Mean (SD) age in years • Bimekizumab: 45.9 (14.2) • Secukinumab: 44.0 (14.7) N (%) female • Bimekizumab: 122 (32.7) • Secukinumab: 135 (36.5) N (%) White • Bimekizumab: 347 (93.0) • Secukinumab: 348 (94.1)	Mean (SD) duration of psoriasis in years • Bimekizumab: 18.4 (13.1) • Secukinumab: 17.2 (12.3) Mean (SD) PASI • Bimekizumab: 20.2 (7.5) • Secukinumab: 19.7 (6.7) N (%) had previous therapy with biologic agent • Bimekizumab: 125 (33.5) • Secukinumab: 119 (32.2)	UCB Pharma
Ritchlin et al. 2020[20] Czech Republic, Germany, Hungary, Poland, Russia, US BE ACTIVE NCT02969525 Moderate	Adults age 18 and older with chronic (≥ 6 months) psoriatic arthritis with a diagnosis of PsA according to CASPAR criteria. Eligible participants had active disease at baseline and had an active psoriatic lesion or documented history of psoriasis. Eligible participants could take concomitant corticosteroids, nonsteroidal anti-inflammatory drugs, or csDMARDs if they took them at a stable dose for at least 2 weeks before baseline. Participants were excluded if they currently used TNF inhibitors.	Mean (SD) age in years • Placebo: 49 (12.1) • Bimekizumab 320 mg: 50.4 (12.1) N (%) female • Placebo: 18 (43) • Bimekizumab 320 mg: 18 (44) N (%) Asian • Placebo: 1 (2) • Bimekizumab 320 mg: 0 (0) N (%) Black • Placebo: 1 (2) • Bimekizumab 320 mg: 0 (0)	Mean (SD) Duration of PsA in years • Placebo: 6.7 (7.0) • Bimekizumab 320 mg: 7.0 (7.2) N (%) BSA >3% (moderate or severe) • Placebo: 28 (66.7) • Bimekizumab: 26 (63.4)	UCB Pharma

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
		N (%) White • Placebo: 40 (95) • Bimekizumab 320 mg: 41 (100)		
Warren et al., 2021[25] Australia, Canada, Czech Republic, Germany, Hungary, Poland, Republic of Korea, Russian Federation, Taiwan, US BE SURE NCT03412747 Moderate	Adults with moderate-to-severe plaque psoriasis ≥6 months' duration defined by PASI ≥ 12, PGA ≥ 3 on a 5-point scale, and BSA involvement ≥ 10%. Participants were excluded if they had history of prior treatment with bimekizumab or adalimumab and if they had primary failure to any anti-interleukin-17 biologic agent or to more than 1 biologic agent of any other class.	Mean (SD) age in years • Bimekizumab every 4 weeks: 45.3 (13.2) • Bimekizumab every 4 weeks then every 8 weeks: 44.0 (13.5) • Adalimumab: 45.5 (14.3) 150 (31.4%) Female 421 (88.1%) White	Mean (SD) duration of psoriasis in years • Bimekizumab every 4 weeks: 20.4 (13.2) • Bimekizumab every 4 weeks then every 8 weeks: 17.3 (10.9) • Adalimumab: 16.2 (11.9) Mean (SD) PASI • Bimekizumab every 4 weeks: 20.5 (6.9) • Bimekizumab every 4 weeks then every 8 weeks: 19.9 (6.1) • Adalimumab: 19.0 (5.9)	UCB Pharma
Warren et al., 2021[19] Canada, France, Germany, Italy, Netherlands, Poland, Spain, UK, US IMMerge NCT03478787 Moderate	Adults with moderate-to-severe chronic plaque psoriasis with or without psoriatic arthritis defined by PASI ≥ 12, sPGA ≥ 3, and BSA involvement ≥ 10%. Eligible participants were also candidates for systemic therapy. Participants were ineligible if they had a history of erythrodermic psoriasis, generalized or localized pustular psoriasis, medication-induced psoriasis, or new-onset guttate psoriasis. Participants were also ineligible if they had a history of inflammatory bowel disease, chronic	Mean (SD) age in years 47.1 (14.1) 114 (35%) Female N (%) White: • Risankizumab: 151 (92.1) • Secukinumab: 144 (88.3) N (%) Black/African American: • Risankizumab: 6 (3.7) • Secukinumab: 6 (3.7) N (%) Asian: • Risankizumab: 6 (3.7) • Secukinumab: 11 (6.7)	Mean (SD) PASI 19.9 (7.2) N (%) sPGA score of 3 277 (84.7) Mean (SD) duration of psoriasis in years • Risankizumab: 18.6 (12.6) • Secukinumab: 17.4 (13.2)	AbbVie

Author, Year Country Trial Name Trial Number Risk of Bias	Population	Age Gender Race/Ethnicity	Other Population Characteristics	Funding
	infections, active systemic infection, history of malignancy or previous exposure to risankizumab or secukinumab.	N (%) other: • Risankizumab: 1 (0.6) • Secukinumab: 2 (1.2) N (%) Hispanic or Latino ethnicity: • Risankizumab: 37 (22.6) • Secukinumab: 34 (20.9)		

Abbreviations: bDMARD: biologic disease-modifying antirheumatic drug; BMI: body mass index; BSA: body surface area; CASPAR: Classification for Psoriatic Arthritis; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMARD: disease-modifying antirheumatic drug; HAQ: Health Assessment Questionnaire; HIV: human immunodeficiency virus; IGA: Investigator's Global Assessment; IL: interleukin; IQR: interquartile range; JAK: janus kinase; NCT: US National Clinical Trial; NR: not reported; NSAID: nonsteroidal anti-inflammatory drug; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PtGA: Patient's Global Assessment; PGA: Physicians Global Assessment; PsA: psoriatic arthritis; QoL: quality of life; RCT: randomized controlled trial; SD: standard deviation; SPARCC EI: Spondyloarthritis Research Consortium of Canada Enthesitis Index; TB: tuberculosis; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha; US: United States; UV: ultraviolet; vs.: versus.

Table B2. Evidence Table for RCTs of TIMs for Plaque Psoriasis and Psoriatic Arthritis (Intervention and Results)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Al Mutairi et al., 2020[23] NA Moderate	Ixekizumab 160 mg SC at weeks 0, and then 80 mg SC every 2 weeks until week 12 followed by 80 mg SC every 4 weeks until week 24 Secukinumab 300 mg SC once weekly for first 4 weeks followed by once every 4 weeks until week 24	Ixekizumab: 28 Secukinumab: 26 Total: 54	*At 24 weeks* **N (%) sPGA 0 or 1** Ixekizumab: 24 (85.7) Secukinumab: 22 (84.6) Reported *P* = .21 Calculated RR (95% CI): 1.01 (0.81 to 1.3), *P* = .91 **N (%) sPGA 0** Ixekizumab: 19 (68.0) Secukinumab: 17 (65.9) Reported *P* = .17 Calculated RR (95% CI): 1.04 (0.71 to 1.5), *P* = .85 **N (%) GPSS total score with 3-point baseline improvement** Ixekizumab: 20 (69.7) Secukinumab: 18 (68.3) Calculated RR (95% CI): 1.03 (0.73 to 1.5) **N (%) impaired sexual function** Ixekizumab: 4 (14.3) Secukinumab: 3 (11.5) Calculated RR (95% CI): 1.2 (0.31 to 5.0)	N (%) with AE • Ixekizumab: 19 (67.9) • Secukinumab: 17 (65.4) Calculated RR (95% CI): 1.04 (0.71 to 1.5) N (%) injection-site reactions • Ixekizumab: 5 (17.9) • Secukinumab: 4 (15.4) Calculated RR (95% CI): 1.2 (0.35 to 3.9) 0 SAEs in all groups 0 discontinuations due to AEs in all groups	N (%) mild to moderate infections and infestations • Ixekizumab: 7 (25) • Secukinumab: 6 (23.1) 0 deaths in all groups
Araujo et al., 2019[43] ECLIPSA High	Ustekinumab 45 m SC (body weight < 100 kg) or 90 mg (body weight > 100 kg body weight) at weeks 0, 4, 12, and 24. TNF-α inhibitor at standard approved doses and frequency. The choice of	Ustekinumab: 23 TNF-α inhibitor: 24 (adalimumab: 10, certolizumab: 6; etanercept: 5, infliximab: 3) Total: 47	*Primary outcomes at week 24* **SPARCC EI 0** Ustekinumab: 17*(73.9) TNF-α inhibitor: 10* (41.7); *P* = .018 **SPARCC EI (repeated measures)** *P* = .007 favoring ustekinumab *Secondary outcomes at week 24* **MASES 0** Ustekinumab: 19* (82) TNF-α inhibitor: 12* (50); *P* = .002 **MASES (repeated measures)** *P* = .022 favoring ustekinumab **LEI 0**	NR	NR

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	TNF-α inhibitor was according to patient's preferences related to route and frequency of administration.		Ustekinumab: 18* (78) TNF-α inhibitor: 12*(50); *P* = .032 LEI indices (repeated measures), *P* = 0.074 **TJC 0** Ustekinumab: 12 (54) TNF-α inhibitor: 11 (46); *P** = .78 TJC score (repeated measures), *P* = .889 **SJC 0** Ustekinumab: 14* (59) TNF-α inhibitor: 11* (46); *P** = .38 SJC score (repeated measures), *P* = .957 **PASI 100** Ustekinumab: 14* (59) TNF-α inhibitor: 7* (29); *P* = .039 **PASI 90** Ustekinumab: 20*(86) TNF-α Inhibitor: 7* (29); *P* < .001 **PASI score** (repeated measures) *P* = .03, favoring ustekinumab **MDA 5/7** Ustekinumab: 18* (77) TNF-α Inhibitor: 11* (45); *P* = .04 **SF-36 PCS** (repeated measures), *P* < .001, favoring ustekinumab **SF-36 MCS** (repeated measures), *P* = .509		
Atteno et al., 2010[50] None High	Infliximab 5mg/kg every 6 to 8 weeks, Etanercept 25 mg twice weekly, Adalimumab 40 mg every other week	Infliximab: 30 Etanercept: 36 Adalimumab: 34 Total: 100	*At 1 year* **Median (IQR) PASI** Etanercept: 2 (4.4) Adalimumab: 0.1 (1.90) Infliximab: 0.0 (1) Overall: 0.6 (2) *P* < .01 **Median (IQR) HAQ** Etanercept: 0.1 (0.1) Adalimumab: 0.1 (0.2)	**% AE** Infliximab: 23 Etanercept: 17 Adalimumab: 6 *P* = .001 Calculated RR 0.38, 95% CI, 0.17 to 0.84, for adalimumab vs. etanercept: Calculated RR, 0.23;	No cases of tuberculosis or demyelinating disease were reported.

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Infliximab: 0.1 (0) Overall: 0.1 (0.1) *P* = .60 **Median (IQR) tender joints** Etanercept: 1(1) Adalimumab: 1 (2) Infliximab: 1 (1.8) Overall: 1(1) *P* = .12 **Median (IQR) swollen joints** Etanercept: 0 (1) Adalimumab (0.5 (1) Infliximab: 1 (1) Overall: 0 (1) *P* = .23 **% ACR20 Response** Etanercept: 72 Adalimumab: 70 Infliximab: 75	95% CI, 0.11 to 0.49, for adalimumab vs. infliximab Calculated RR, 1.6; 95% CI, 1.1 to 2.4 for Infliximab vs. etanercept **SAEs** Two SAEs occurred in the infliximab group (pneumonitis and thrombocytopenia). Both were considered drug related and resolved with drug withdrawal and treatment.	
Bachelez et. al., 2015[62] Valenzuela et al., 2016[63] OPT Moderate	Tofacitinib 5 mg twice daily, Tofacitinib 10 mg twice daily, Etanercept 50 mg subcutaneously twice weekly Placebo	1,106	*Primary outcomes at week 12* **% PASI 75** 39.5% (tofacitinib 5 mg) vs. 63.6% (tofacitinib 10 mg) vs. 58.8% (etanercept 50 mg) ARD 5 mg vs. etanercept:−19.3, *P* < .001 ARD 10 mg vs. etanercept: 4.8, *P* = .20 **% PGA 0 or 1** 47.1% (tofacitinib 5 mg) 68.2% (tofacitinib 10 mg) 66.3% (etanercept) ARD 5 mg vs. etanercept: −19.2, *P* < .001 ARD 10 mg vs. etanercept: 1.9; *P* = .60 *Secondary outcomes at week 12* **% PASI 90** 21.0 % (tofacitinib 5 mg) 36.1% (tofacitinib 10 mg)	**% treatment-related AE** RR (95% CI vs. tofacitinib) Etanercept 50 mg: 57% Tofacitinib 5 mg: 55% 1.1 (0.92 to 1.2) Tofacitinib 10 mg: 60% 0.96 (0.84 to 1.1) **% serious treatment-related AE** Etanercept 50 mg: 2% Tofacitinib 5 mg: 2% 0.98 (0.35 to 2.8) Tofacitinib 10 mg: 2% 1.1 (0.39 to 3.4)	**% infections and infestations** Tofacitinib 5 mg: 19% Tofacitinib 10 mg: 22% Etanercept 50 mg: 23% **% serious infections** Tofacitinib 5 mg: 1% perforated diverticulitis, extradural abscess Tofacitinib 10

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			32.2% (etanercept) ARD 5 mg vs. etanercept:−11.3, *P* = .0009 ARD 10 mg vs. etanercept: 3.8; *P* = .30 **% PASI 50** 65.7% (tofacitinib 5 mg) 80.6% (tofacitinib 10 mg) 80.3% (etanercept) ARD 5 mg vs. etanercept: −14.6, *P* < .001 ARD 10 mg vs. etanercept: 0.3; *P* = .92 **% DLQI reduction ≥ 5 points** 66.3% (tofacitinib 5 mg) 78.2% (tofacitinib 10 mg) 74.7% etanercept ARD 5 mg vs. etanercept: −8.3; *P* = .03 ARD 10 mg vs. etanercept: 3.5; *P* = .31 **% DLQI 0 or 1** 30.9% (tofacitinib 5 mg) vs. 47.3% (tofacitinib 10 mg) vs. 43.6% (etanercept 50 mg), *P* = NR **Mean (SE) change SF-36 PCS** 4.0 (0.4) (tofacitinib 5 mg) vs. 5.4 (0.4) (tofacitinib 10 mg) vs. 5.0 (0.4) (etanercept 50 mg), *P* = NR **Mean (SE) change SF-36 MCS** 5.2 (0.5) (tofacitinib 5 mg) vs. 7.6 (0.5) (tofacitinib 10 mg) vs. 5.9 (0.5) (etanercept 50 mg), *P* = NR **PtGA:** 30.4% (tofacitinib 5 mg) vs. 51.8% (tofacitinib 10 mg) vs. 49.0% (etanercept 50 mg), *P* = NR, rates reported as 'similar' **% ISI (little or no itch):** 55.6% (tofacitinib 5 mg) vs. 68.6% (tofacitinib 10 mg) vs. 57.4% (etanercept 50 mg), *P* < 0.05 for 10 mg tofacitinib vs. etanercept	**% severe treatment-related AE** Etanercept 50 mg: 2% Tofacitinib 5 mg: 2% Tofacitinib 10 mg: 2% **% withdrawal of treatment due to AE** Etanercept 50 mg: 3% Tofacitinib 5 mg: 1% 3.6 (1.01 to 12.8) Tofacitinib 10 mg: 3% 1.1 (0.47 to 2.5)	mg: 1% pneumonia, paronychia Etanercept 50 mg: 1% bronchitis, perineal abscess **% gastro-intestinal disorders** Tofacitinib 5 mg: 9% Tofacitinib 10 mg: 9% Etanercept 50 mg: 9% **General disorders and administration site conditions** (among others: Injection-site erythema, Injection-site reaction) Tofacitinib 5 mg: 6% Tofacitinib 10 mg: 6% Etanercept 50 mg: 15% **Major cardiac events** Tofacitinib 5 mg: 0.3%

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
					Myocardial Infarction Tofacitinib 10 mg: 0 Etanercept 50 mg: 0.3%; Stroke or transient ischemic attack **Mortality** 0 in all groups
Bagel et al., 2018[39] Bagel et al., 2021[77] CLARITY Moderate	Secukinumab 300 mg SC at baseline, weeks 1, 2, and 3, and then every 4 weeks from weeks 4 Ustekinumab SC 45 mg (for participants weighing ≤ 100 kg) or 90 mg (for participants weighing participants > 10 0 kg) at baseline, week 4, and then every 12 weeks	Secukinumab 300 mg: 550 Ustekinumab 45/90 mg: 552 Total: 1,102	*Primary outcomes at week 12* **N (%) PASI 90** Secukinumab: 366 (66.5) Ustekinumab: 264 (47.9) *P* < .001 **N (%) IGA 0 or 1** Secukinumab: 398 (72.3) Ustekinumab: 264 (55.4) *P* < .001 *Secondary outcomes* **% PASI 90 at week 16** Secukinumab: 76.6 Ustekinumab: 54.2 *P* < .001 **% PASI 90 at week 52** Secukinumab: 73.2 Ustekinumab: 59.8 OR 1.84; 95% CI, 1.41 to 2.41 **% PASI 75 at week 12** Secukinumab: 88.0 Ustekinumab: 74.2 *P* < .001 **% PASI 75 at week 16** Secukinumab: 91.7 Ustekinumab: 79.8	**N (%) TEAE at 16 weeks** Secukinumab: 261 (47.5) Ustekinumab: 256 (46.4) Calculated RR, 1.0; 95% CI, 0.90 to 1.2 **N (%) serious TEAE at 16 weeks** Secukinumab: 14 (2.5) Ustekinumab: 9 (1.6) Calculated RR, 1.6; 95% CI, 0.68 to 3.6 **N (%) withdrawal due to AEs at 16 weeks** Secukinumab: 11 (2.0) Ustekinumab: 7 (1.3) Calculated RR, 1.6; 95% CI, 0.62 to 4.0 **N (%) TEAE at 52 weeks** Secukinumab: 377 (68.5) Ustekinumab: 390	**N (%) infections and infestations at 16 weeks** Secukinumab: 122 (22.2) Ustekinumab: 117 (21.2) Calculated RR, 1.0; 95% CI, 0.84 to 1.3 **N (%) infections and infestations at 52 weeks** Secukinumab: 236 (42.9%) Ustekinumab: 219 (39.7%) Calculated RR, 1.08 95% CI, 0.94 to 1.25 There were 2 deaths, 1 due to acute intoxication by

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			% PASI 75 at week 52 Secukinumab: 89.0 Ustekinumab: 82.1 OR 1.74; 95 % CI, 1.21 to 2.5 **% PASI 100 at week 12** Secukinumab: 38.1 Ustekinumab: 20.1 *P* < .001 **% PASI 100 at week 16** Secukinumab: 45.3 Ustekinumab: 26.7 *P* < .001 **% PASI 100 at week 52** Secukinumab: 48.9 Ustekinumab: 33.5 OR 1.92; 95% CI, 1.48 to 2.47 **% IGA 0 or 1 at week 16** Secukinumab: 78.6 Ustekinumab: 59.1 *P* < .001 **% IGA 0 or 1 at week 52** Secukinumab: 76.0 Ustekinumab: 60.2 OR 2.12; 95% CI, 1.61 to 2.79 **% DLQI 0 or 1 at week 12** Secukinumab: 64.0 Ustekinumab: 51.7 *P* < .001 **% DLQI 0 or 1 at week 16** Secukinumab: 68.4 Ustekinumab: 55.9 *P* < .001 **% DLQI 0 or 1 at week 52** Secukinumab: 69.9 Ustekinumab: 62.2	(70.7) Calculated RR, 0.97 95% CI, 0.90 to 1.05 **N (%) SAEs at 52 weeks** Secukinumab: 29 (5.3) Ustekinumab: 21 (3.9) Calculated RR: 1.4; 95% CI, 0.80 to 2.4 **N (%) withdrawal due to AEs at 52 weeks** Secukinumab: 21 (3.8) Ustekinumab: 13 (2.4) Calculated RR, 1.62 95% CI, 0.82 to 3.21	cocaine and another due to sudden cardiac death (had hypertension and heart disease).

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			P = .003		
Blauvelt et al., 2020[17] Blauvelt et al., 2021[36] IXORA-R (NCT03573323) Moderate	Ixekizumab 80 mg SC (after 160 mg starting dose at week 0) every 2 weeks until week 12 then every 4 weeks until week 24 Guselkumab 100 mg SC at week 0, 4, 12, and 20	Ixekizumab: 520 Guselkumab: 507 Total: 1,027	At 12 weeks Primary outcome N (%) PASI 100 Ixekizumab: 215 (41) Guselkumab: 126 (25) Reported ARD (95% CI): 16.5 (10.8 to 22.2); *P* < .001 Reported OR (95% CI): 2.1 (1.6 to 2.8) Calculated RR (95% CI): 1.7 (1.4 to 2.0) Secondary outcomes N (%) sPGA 0 Ixekizumab: 218 (42) Guselkumab: 128 (25) Reported ARD (95% CI): 16.7 (11.0 to 22.4); *P* < .001 Reported OR (95% CI): 2.2 (1.6 to 2.8) Calculated RR (95% CI): 1.7 (1.4 to 2.0) Significant differences favoring ixekizumab reported between groups for % achieving DLQI 0 or 1, itch NRS 0, and PtGA 0 or 1 (depicted on figures only, actual values NR) At 24 weeks PASI 100 Ixekizumab: 260 (50) Guselkumab: 265 (52) Reported ARD (95% CI): −2.3 (−8.4 to 3.8), *P* = .41 Calculated RR (95% CI): 0.96 (0.85 to 1.1)	At 24 weeks N (%) any TEAE Ixekizumab: 323 (62) Guselkumab: 286 (57) Calculated RR (95% CI): 1.1 (0.99 to 1.2) N (%) SAEs Ixekizumab: 18 (3) Guselkumab: 16 (3) Calculated RR (95% CI): 1.1 (0.6 to 2.1) N (%) discontinuations due to TEAE Ixekizumab: 15 (3) Guselkumab: 8 (2) Calculated RR (95% CI): 1.8 (0.8 to 4.3) N (%) injection-site reaction Ixekizumab: 67 (13) Guselkumab: 19 (4) Calculated RR (95% CI): 3.4 (2.1 to 5.6)	N (%) infections Ixekizumab: 162 (31) Guselkumab: 143 (28) N (%) malignancies Ixekizumab: 2 (0.4) Guselkumab: 2 (0.4) N (%) major adverse cardiac event Ixekizumab: 4 (0.8) Guselkumab: 2 (0.4) Mortality 0 in all groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			No significant differences in PASI 50, PASI 75, PASI 90, sPGA 0, sPGA 0 or 1, Pat GA 0 or 1, DLQI 0 or 1, itch NRS 0 (depicted on figures only, actual values NR) Time to PASI 90 (weeks) Ixekizumab: median 8 .0 (95% CI, 6.4 to 8.1) Guselkumab: 10.1 (95% CI, 10.1 to 10.7)		
Blauvelt et al., 2017[69] Papp et al., 2018[70] VOYAGE-1 Moderate	Guselkumab 100 mg SC at 0, 4, 12 weeks Adalimumab 80 mg SC at week 0 and 40 mg at weeks 1 and every 2 weeks after This study also included a placebo arm.	Guselkumab: 329 Adalimumab: 334 Total: 837	*Primary outcomes at week 16* **N (%) IGA 0 or 1** Guselkumab: 280 (85.1) Adalimumab: 220 (65.9) ARD*. 19.2%; 95% CI, 12.9% to 25.6% Calculated RR, 1.3; 95 %CI, 1.2 to 1.4 **N (%) PASI 90** Guselkumab: 241 (73.3) Adalimumab: 166 (49.7) ARD*, 23.6%; 95% CI, 16.4% to 30.7% Calculated RR, 1.5; 95 %CI, 1.3 to 1.7 *Secondary outcomes at week 16* **N (%) PASI 100** Guselkumab: 123 (37.4) Adalimumab: 57 (17.1) ARD*, 20.3%; 95% CI, 13.7% to 26.9% Calculated RR, 2.2; 95 %CI, 1.7 to 2.9 **N (%) IGA 0** Guselkumab: 157 (47.7) Adalimumab: 88 (26.3) ARD*, 21.4%; 95% CI, 14.2% to 28.6% Calculated RR 1.8 (95 %CI, 1.5 to 2.2) **N (%) PASI 75** Guselkumab: 300 (91.2) Adalimumab: 244 (73.1) ARD*, 18.1%; 95% CI, 12.5% to 23.8% Calculated RR, 1.2; 95 %CI, 1.2 to 1.3 **Mean (SD) change in DLQI**	*At 16 weeks* **N (%) AEs** Guselkumab: 170 (51.7) Adalimumab: 170 (51.1) Calculated RR 1.01 (95% CI, 0.87 to 1.17) **N (%) SAEs** Guselkumab: 8 (2.4) Adalimumab: 6 (1.8) Calculated RR, 1.35 (95% CI, 0.47 to 3.9) **N (%) withdrawal because of AE** Guselkumab: 4 (1.2) Adalimumab: 3 (0.9) Calculated RR, 1.35; 95 % CI, 0.30 to 6.0	*At 16 weeks* **N (%) infections** Guselkumab: 85 (25.8) Adalimumab: 85 (25.5) Calculated RR, 1.01; 95 % CI, 0.78 to 1.3 **N (%) injection-site erythema** Guselkumab: 6 (1.8) Adalimumab: 15 (4.5) Calculated RR, 0.40; 95% CI, 0.16 to 1.03

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Guselkumab: −11.2 (7.2) Adalimumab: −9.3 (7.8) AMD, −1.9; 95% CI, −3.1 to −0.74; *P* = .001 **Mean (SD) change in PSSD symptom score** Guselkumab: −41.9 (24.6) Adalimumab: −35.4 (28.5) AMD, −6.5; 95% CI, −11.1 to −1.9; *P* = .006 **Mean (SD) change in PSSD sign score** Guselkumab: −44.6 (22) Adalimumab: −39.7 (26.4) AMD, −4.9; 95% CI, −9.1 to −0.70; *P* = .02		
Blauvelt et al., 2017[41] Blauvelt et al., 2016[42] Thaci et al., 2015[40] CLEAR Moderate	Secukinumab 300 mg SC at weeks 0, 1, 2, and 3 then every 4 weeks Ustekinumab SC 45 mg or 90 mg (if patient weight more than 100 kg) at weeks 0, 4, and then every 12 weeks 52 weeks	Secukinumab: 337 Ustekinumab: 339 Total: 676	*Primary outcome at week 16* **PASI 90** 79.0% (secukinumab) vs. 57.6% (ustekinumab), *P* < .001 *Secondary outcomes at week 16* **PASI 100** 44.3% (secukinumab) vs. 28.4% (ustekinumab); *P* < .001 **PASI 75** 93.1% (secukinumab) vs. 82.8% (ustekinumab); *P* < .001 **IGA 0 or + an improvement of ≥ 2 points** 82.9% (secukinumab) vs. 67.5% (ustekinumab); *P* < .001 **DLQI 0 or 1** 71.9% (secukinumab) vs. 57.4% (ustekinumab); *P* < .001 **Change in mean (SD) symptom scores** **Pain** Secukinumab: −3.3 (0.8) vs. ustekinumab: −2.8 (1.0); *P* = .0414 **Itching** Secukinumab −5.0 (1.2) vs. ustekinumab −4.6 (1.6); *P* = .0053 **Scaling** Secukinumab −5.7 (0.8) vs. ustekinumab −5.2 (1.3); *P* < .001 *Outcomes at week 52* **PASI 90** 74.9% (secukinumab) vs. 60.6%	*At week 16* **N (%) AE** Secukinumab: 215 (64) Ustekinumab: 196 (58) Calculated RR, 1.1; 95% CI, 0.98 to 1.24 **N (%) SAE** Secukinumab: 10 (3) Ustekinumab: 10 (3) Calculated RR, 1.00; 95% CI, 0.42 to 2.38 **N (%) withdrawals because of AE** Secukinumab: 3 (1) Ustekinumab: 4 (1) Calculated RR, 0.75; 95% CI, 0.17 to 3.34 *At week 52* **N (%) AE** Secukinumab: 286 (85) Ustekinumab: 278 (83) Calculated RR, 1.03, 95% CI, 0.97 to 1.10 **N (%) SAEs**	*At week 16* **N (%) infections and infestations** Secukinumab: 98 (29) Ustekinumab: 85 (25)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			(ustekinumab); *P* < .001 **PASI 100** 44.9% (secukinumab) vs. 36.7% (ustekinumab); *P* = .03 **IGA 0 or 1** Actual values NR, but secukinumab > ustekinumab (*P* < .001) **PASI 75** Actual values NR, but secukinumab > ustekinumab (*P* < .001) **DLQI (0 or 1)** 71.6% (secukinumab) vs. 59.2% (ustekinumab); *P* = .008 **Change in mean (SD) symptoms scores**, pain, itching, scaling only reported on figures, all were reported as statistically significant differences favoring secukinumab **EQ-5D-3L Visual Analog Scale (mean change)** 13.8 (secukinumab) vs. 10.6 (ustekinumab); *P* = .03 **WPAI-PSO subscales** **Absenteeism** −53% (secukinumab) vs. −39% (ustekinumab); *P* NS **Presenteeism** −89% (secukinumab) vs. −65% (ustekinumab); *P* < .01 **Work productivity loss** −81% (secukinumab) vs. −57% (ustekinumab); *P* < .01 **Overall daily activity impairment** −87% (secukinumab) vs. −76% (ustekinumab); *P* < .01)	Secukinumab: 30 (9) Ustekinumab: 27 (8) Calculated RR, 1.1; 95% CI, 0.68 to 1.80 **N (%) withdrawals because of AEs** Secukinumab: 10 (3) Ustekinumab: 9 (3) Calculated RR, 1.1; 95% CI, 0.46 to 2.70	
De Vries et al., 2017[64] PIECE High	Etanercept 50 mg subcutaneous twice weekly Infliximab 5 mg /kg intravenously at weeks 0, 2, 6 and every 8 weeks thereafter 24 weeks	Etanercept: 23 Infliximab: 25 Total: 48	*Primary outcome at week 24* **PASI 75** 72% (infliximab) vs. 35% (etanercept), *P* = .01 *Secondary outcomes at 24 weeks* **Skindex-17 relative reduction of symptoms** 29.9% (infliximab) vs. 25.1% (etanercept), *P* = .01 **Relative improvement on SF-36 PCS** 6.7% (infliximab) vs. 9.9% (etanercept), *P* = .32 **Relative improvement on SF-36 MCS** 0.6%	**% AE** Infliximab: 96 Etanercept: 100 SAEs: Infliximab: 0.5 Etanercept: 0.7 **% AE leading to drug withdrawal** Infliximab: 12.0	**% injection-site or infusion reactions** Infliximab: 24 Etanercept: 9

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	(induction phase)		(infliximab) vs. 2.2% (etanercept), *P* = .58	Etanercept: 8.7	
Glatt et al., 2017[53] NCT02529956 Moderate	Participants were randomized to receive a one-time infusion of placebo, bimekizumab 8 mg, 40 mg, 160 mg, 480 mg, or 640 mg over 60 minutes duration	Placebo: 13 Bimekizumab 8 mg: 4 Bimekizumab 40 mg: 4 Bimekizumab 160 mg: 6 Bimekizumab 480 mg: 6 Bimekizumab 640 mg: 6 Total: 39	**Mean lesion severity score** reduction of >80% was observed in the 640 mg and 480 mg bimekizumab groups by week 2. Maximal reductions for most doses achieved by week 8 and maintained through week 16. The 95 % CI for placebo and bimekizumab 40 mg, 160 mg, 480 mg, and 640 mg groups did not overlap by week 2; at did not overlap for the 640 mg at any time point. **PASI and PGA:** statistically significant % change from baseline for 160 mg, 480 mg, and 640-mg dosages vs. placebo at nearly all time points. (actual values NR, depicted on a figure)	**N (%) TEAE** Placebo: 10 (76.9) Bimekizumab: 22 (84.6) Calculated RR, 1.1; 95% CI, 0.78 to 1.5 **N (%) with treatment-related TEAE** Placebo: 4 (30.8) Bimekizumab: 12 (46.2) **N (%) with serious TEAEs** Placebo: 0 (0) Bimekizumab: 1 (3.8) Unable to calculate RR **N (%) with severe TEAEs** Placebo: 0 (0) Bimekizumab: 0 (0) Unable to calculate RR **N (%) withdrawals due to TEAEs** Placebo: 0 (0) Bimekizumab: 0(0) RR*, 1.0; 95% CI, 0.0004 to 249	**N (%) deaths:** 0 (0) Commonly reported AEs occurring in >10% of all subjects receiving bimekizumab: headache, oropharyngeal pain, nasopharyngitis
Gordon et al., 2021[22] BE READY	Bimekizumab 320 mg SC every 4 weeks for 16 weeks	Bimekizumab: 349 Placebo: 86 Total: 435	At 16 weeks Primary outcome N (%) PASI 90 Bimekizumab: 317 (91)	At week 16 **N (%) any TEAE** Bimekizumab: 213 (61) Placebo: 35 (41)	N (%) serious infections Bimekizumab: 2 (1)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
(NCT03410992) Moderate	Placebo SC every 4 weeks for 16 weeks This study also included a withdrawal period from 16 weeks to 56 weeks where responders randomized to bimekizumab were rerandomized to placebo, bimekizumab every 4 weeks or bimekizumab every 8 weeks; these analyses were not included in this update		Placebo: 1 (1) Reported OR (95% CI): 496.3 (82.8 to 2975.1), *P* < .0001 Calculated RR (95% CI): 78.1 (11.1 to 548.3) N (%) IGA 0 or 1 Bimekizumab: 323 (93) Placebo: 1 (1) Reported OR (95% CI): 657.3 (105.8 to 4083.3), *P* < .0001 Calculated RR (95% CI): 79.6 (11.3 to 558.7) N (%) PASI 100 Bimekizumab: 238 (68) Placebo: 1 (1) Reported OR (95% CI): 220 (28.8 to 1683.6), *P* < .0001 Calculated RR (95% CI): 58.7 (8.3 to 412.1) N (%) IGA 0 Bimekizumab: 243 (70) Placebo: 1 (1) Reported OR (95% CI): 224.7 (30.1 to 1,676.4), *P* < .0001 Calculated RR (95% CI): 59.9 (8.5 to 420.7) N (%) P-SIM pain response (among those with baseline score ≥1.98) Bimekizumab: 201 (79) Placebo: 6 (9) Reported OR (95% CI): 34.3 (14.2 to 82.9), *P* < .0001 Calculated RR (95% CI): 8.8 (4.09 to 18.9) N (%) P-SIM itch response (among those with baseline score ≥2.39) Bimekizumab: 210 (76) Placebo: 4 (6) Reported OR (95% CI): 43.5 (15.7 to 120.3), *P* < .0001	Calculated RR (95% CI): 1.5 (1.1 to 2.0) **N (%) serious TEAE** Bimekizumab: 6 (2) Placebo: 2 (2) Calculated RR (95% CI): 0.74 (0.15 to 3.6) N (%) discontinuations due to TEAE Bimekizumab: 3 (1) Placebo: 0 (0) Calculated RR (95% CI): Unable to calculate 0 events in 1 group	Placebo: 0 (0) N (%) malignancies Bimekizumab: 1 (0.29) Placebo: 0 (0) N (%) nonmelanoma skin cancer Bimekizumab: 1 (0.29) Placebo: 0 (0) Adjudicated major adverse cardiac events 0 in all groups Mortality 0 in all groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Calculated RR (95% CI): 13.6 (5.2 to 35.3), *P* <.0000001 N (%) P-SIM scaling response (among those with baseline score ≥2.86) Bimekizumab: 223 (78) Placebo: 4 (6) Reported OR (95% CI): 60.9 (20.6 to 180.7), *P* < .0001 Calculated RR (95% CI): 13.7 (5.2 to 35.4) N (%) DLQI 0 or 1 Bimekizumab: 264 (75.6) Placebo: 5 (5.8) Reported *P* < .0001 Calculated RR (95% CI): 13.0 (5.5 to 30.5)		
Gordon et al., 2018[67] Augustin et al., 2020[78] UltIMMa-1 UltIMMa-2 Moderate	Risankizumab 150 mg SC at weeks 0, 4, 16, 28 and 40, Ustekinumab 90 mg (if body weight >100kg) or 45 mg (if body weight ≤100 kg) at week 0, 4, 16, 28, and 40	Risankizumab: 304 Ustekinumab: 100 Total: 506 (including 102 randomized to placebo)	***UltIMMA-1*** *Primary outcomes at 16 weeks* **N (%) PASI 90** Risankizumab: 229 (75.3) Ustekinumab: 42 (42.0) Difference from ustekinumab (95% CI) 33.5% (22.7% to 44.3%), *P* < .001 **N (%) PGA 0 or 1** Risankizumab: 267 (87.8) Ustekinumab: 63 (63.0) Difference from ustekinumab (95% CI) 25.1% (15.2% to 35.0%), *P* < .001 *Secondary outcomes at 16 weeks* **N (%) PGA 0** Risankizumab: 112 (36.8) Ustekinumab: 14 (14.0) Difference from ustekinumab (95% CI) 22.9% (14.3% to 31.6%), *P* < .001 **N (%) PASI 100** Risankizumab: 109 (35.9) Ustekinumab: 12 (12.0), Difference from	***UltIMMA-1*** *Weeks 0 to 16* **N (%) AE** Risankizumab: 151 (49.7) Ustekinumab: 50 (50.0) *RR* (95% CI) 0.99 (0.79 to 1.2) **N (%) SAE** Risankizumab: 7 (2.3) Ustekinumab: 8 (8.0) *RR* (95% CI) 0.29 (0.11 to 0.77) **N (%) severe AE** Risankizumab: 6 (2.0) Ustekinumab: 3 (3.0) **N (%) AE leading to withdrawal** Risankizumab: 2 (0.7) Ustekinumab: 2 (2.0)	***UltIMMA-1*** *Weeks 0 to 16* **N (%) infections** Risankizumab: 75 (24.7) Ustekinumab: 20 (20.0) **N (%) deaths** Risankizumab: 0 (0) Ustekinumab: 0 (0) *Weeks 17 to 52* **N (%) infections** Risankizumab: 112 (37.7) Ustekinumab: 41 (41.4) **N (%) deaths** Risankizumab: 0

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			ustekinumab (95% CI) 23.8% (15.5% to 32.1%), *P* < .001 **N (%) DLQI 0 or 1** Risankizumab: 200 (65.8) Ustekinumab: 43 (43.0) Difference from ustekinumab (95% CI), 23.0% (11.9% to 34.0%), *P* < .001 **N (%) PSS 0** Risankizumab: 89 (29.3) Ustekinumab: 15 (15.0) Difference from ustekinumab (95% CI) 14.3% (5.8% to 22.8%), *P* = .001 **Mean (SD) change in PSS**, Risankizumab: −5.6 (0.2) Ustekinumab: −4.4 (0.3) Difference (95% CI) −1.2 (−1.9 to −0.4) *Outcomes at 52 weeks* **N (%) PASI 90** Risankizumab: 249 (81.9) Ustekinumab: 44 (44.0) Difference from ustekinumab (95% CI) 38.3% (27.9% to 48.6%), *P* < .001 **N (%) PASI 100** Risankizumab: 171 (56.3) Ustekinumab: 21 (21.0) Difference from ustekinumab (95% CI) 35.1% (25.7% to 44.6%), *P* < .001 **N (%) PGA 0** Risankizumab: 175 (57.6) Ustekinumab: 21 (21.0) Difference from ustekinumab (95% CI) 36.5% (27.0% to 45.9%), *P* < .001 ***UltIMMA-2***	*RR* (95% CI) 0.33 (0.05 to 2.3) *Weeks 17 to 52* **N (%) AE** Risankizumab: 182 (61.3) Ustekinumab: 66 (66.7) *RR* (95% CI) 0.92 (0.78 to 1.1) **N (%) SAE** Risankizumab: 16 (5.4) Ustekinumab: 4 (4.0) *RR* (95% CI) 1.3 (0.46 to 3.9) **N (%) severe AE** Risankizumab: 13 (4.4) Ustekinumab: 1 (1.0) **N (%) AE leading to drug withdrawal** Risankizumab: 0 (0) Ustekinumab: 0 (0) *RR* (95% CI) 0.33 (0.001 to 84.9) ***UltIMMA-2*** *Weeks 0 to 16* **N (%) AE** Risankizumab: 134 (45.6) Ustekinumab: 53 (53.5) *RR* (95% CI) 0.85 (0.68 to 1.1) **N (%) SAE**	(0) Ustekinumab: 0 (0) ***UltIMMA-2*** *Weeks 0 to 16* **N (%) infections** Risankizumab: 56 (19.0) Ustekinumab: 20 (20.2) **N (%) deaths** Risankizumab: 1 (0.3) Ustekinumab: 0 (0) *Weeks 17 to 52* **N (%) infections** Risankizumab: 101 (34.7) Ustekinumab: 46 (48.9) **N (%) deaths** Risankizumab: 1 (0.3) Ustekinumab: 0 (0)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Primary outcome at week 16 **N (%) PASI 90** Risankizumab: 220 (74.8) Ustekinumab: 47 (47.5) Difference from ustekinumab (95% CI), *P* value 27.6% (16.7% to 38.5%), <.001 **N (%) PGA 0 or 1** Risankizumab: 246 (83.7) Ustekinumab: 61 (61.6) Difference from ustekinumab (95% CI), *P* value 22.3% (12.0% to 32.5%), <.001 *Secondary outcomes at week 16* **N (%) PGA 0** Risankizumab: 150 (51.0) Ustekinumab: 25 (25.3) Difference from ustekinumab (95% CI), *P* value 26.3% (16.1% to 36.4%), < .001 **N (%) PASI 100** Risankizumab: 149 (50.7) Ustekinumab: 24 (24.2) Difference from ustekinumab (95% CI), *P* value 27.0% (17.0% to 37.0%), <.001 **N (%) DLQI 0 or 1** Risankizumab: 196 (66.7) Ustekinumab: 46 (46.5) Difference from ustekinumab (95% CI), *P* value 20.2% (9.1% to 31.4%), <.001 **N (%) PSS 0** Risankizumab: 92 (31.3) Ustekinumab: 15 (15.2) Difference from ustekinumab (95% CI), *P* value 16.1% (7.5% to 24.8%), .0003 **Mean (SD) change in PSS**, difference (95% CI) Risankizumab: −6.4 (0.2) Ustekinumab: −5.6 (0.3)	Risankizumab: 6 (2.0) Ustekinumab: 3 (3.0) *RR* (95% CI) 0.67 (0.17 to 2.6) **N (%) severe AE** Risankizumab: 7 (2.4) Ustekinumab: 6 (6.1) **N (%) AE leading to drug withdrawal** Risankizumab: 1 (0.3) Ustekinumab: 0 (0) *RR* (95% CI) 1.4 (0.02 to 107.4) *Weeks 17 to 52* **N (%) AE** Risankizumab: 162 (55.7) Ustekinumab: 70 (74.5) *RR* (95% CI) 0.75 (0.64 to 0.87) **N (%) SAE** Risankizumab: 13 (4.5), Ustekinumab: 4 (4.3) *RR* (95% CI) 1.1 (0.35 to 3.1) **N (%) severe AE** Risankizumab: 5 (1.7) Ustekinumab: 1 (1.1) **N (%) AE leading to drug withdrawal** Risankizumab: 2 (0.7) Ustekinumab: 2 (2.1) *RR* (95% CI) 0.32 (0.05 to 2.3)	

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			−0.8 (−1.6 to −0.1) *At 52 weeks* **N (%) PASI 90**, difference from ustekinumab (95% CI), *P* value Risankizumab: 237 (80.6) Ustekinumab: 50 (50.5) 30.2% (19.6% to 40.9%), <.001 **N (%) PASI 100**, difference from ustekinumab (95% CI), *P* value Risankizumab: 175 (59.5) Ustekinumab: 30 (30.3) 29.5% (18.9% to 40.1%), <.001 **N (%) PGA 0**, difference from ustekinumab (95% CI), *P* value Risankizumab: 175 (59.5) Ustekinumab: 30 (30.3) 29.5% (18.9% to 40.1%), <.001 UltIMMA-1 and UltIMMA-2 *At 16 weeks* **N (%) achieving MICD on the EQ-5D-5L** Risankizumab: 249/597 (41.7) Ustekinumab: 62/197 (31.5) *P* = .01 *At 52 weeks* **% achieving MICD on the EQ-5D-5L** Risankizumab: 44.4 Ustekinumab: 32.0 *P* = .002		
Gordon et al., 2015[74] X-PLORE Moderate	Adalimumab 80 mg at week 0 and 40 mg at week 1 and every other week through week 39	Placebo: 42 Adalimumab 40 mg: 43 Guselkumab 5 mg: 41 Guselkumab 15	*Primary outcomes at week 16* **N (%) PGA score 0 or 1** Between-group difference in percentage points (95% CI) vs. adalimumab Adalimumab: 25 (58); NA Guselkumab 5 mg: 14 (34); NR	**N (%) AE** Guselkumab: 103 (50) Adalimumab: 24 (56) Calculated RR, 0.89; 95% CI, 0.66 to 1.2 **N (%) SAE**	**N (%) infection** Guselkumab: 41 (20) Adalimumab: 5 (12) Calculated RR,

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	Guselkumab 5 mg at weeks 0 and 4 and every 12 weeks thereafter Guselkumab 15 mg every 8 weeks Guselkumab 50 mg at weeks 0 and 4 and every 12 weeks thereafter Guselkumab 100 mg every 8 weeks Guselkumab 200 mg at weeks 0 and 4 and every 12 weeks thereafter. This trial also included a placebo arm.	mg: 41 Guselkumab 50 mg: 42 Guselkumab 100 mg: 42 Guselkumab 200 mg: 42 Total: 293	Guselkumab 15 mg: 25 (61); NR Guselkumab 50 mg: 33 (79); 20% (2% to 39%) Guselkumab 100 mg: 36 (86); 28% (10% to 46%) Guselkumab 200 mg: 35 (83); 25% (7% to 44%) *Secondary outcomes at week 16* **N (%) PASI 75** Between-group difference in percentage points (95%CI)* vs. adalimumab Adalimumab: 30 (70); NA Guselkumab 5 mg: 18 (44); NR Guselkumab 15 mg: 31 (76); NR Guselkumab 50 mg: 34 (81); 11.2% (–7.0% to 29.3%) Guselkumab 100 mg: 33 (79); 8.8% (–9.7% to 27.3%) Guselkumab 200 mg: 34 (81); 11.2% (–7.0% to 29.3%) **N (%) PASI 90** Between-group difference in percentage points (95%CI)* vs. adalimumab Adalimumab: 19 (44); NA Guselkumab 5 mg: 14 (34); NR Guselkumab 15 mg; 14 (34); NR Guselkumab 50 mg: 19 (45); 1.1% (–20.1% to 22.2%) Guselkumab 100 mg: 26 (62); 17.7% (–3.2% to 38.6%) Guselkumab 200 mg: 24 (57); 13.0% (–8.1% to 34.0%) **N (%) PASI 100** Between-group difference in percentage points (95% CI)* vs. adalimumab Adalimumab: 11 (26); NA Guselkumab 5 mg: 4 (10); NR Guselkumab 15 mg: 5 (12); NR	Guselkumab: 3 (1) Adalimumab: 1 (2) Calculated RR, 0.62; 95% CI, 0.07 to 5.9 **N (%) withdrawal due to AE** Guselkumab: 5 (2) Adalimumab: 3 (7) Calculated RR, 0.35; 95% CI, 0.09 to 1.39	1.7 (95% CI, 0.72 to 4.1) **N (%) injection-site reaction** Guselkumab: 2 (1.0) Adalimumab: 6 (14) Calculated RR, 0.07 (95% CI, 0.01 to 0.33)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Guselkumab 50 mg: 8 (19); −6.5% (−24.2% to 11.1%) Guselkumab 100 mg: 14 (33); 7.8% (−11.6% to 27.1%) Guselkumab 200 mg: 12 (29); 3.0% (−15.9% to 21.9%) **N (%) with DLQI score 0 or 1** Between-group difference in percentage points (95% CI)* vs. adalimumab Adalimumab: 19 (44); NA Guselkumab 5 mg: 10 (26) Guselkumab 15 mg: 14 (34) Guselkumab 50 mg: 17 (41); −3.7% (−24.7% to 17.3%) Guselkumab 100 mg: 25 (60); 15.3% (−5.7% to 36.3%) Guselkumab 200 mg: 26 (62); 17.7% −3.2% to 38.6%) **Mean (SD) change in DLQI score** Adalimumab: −10.1 (9.0) Guselkumab 5 mg: −6.2 (5.2) Guselkumab 15 mg: −10.3 (5.5) Guselkumab 50 mg: −11.1 (7.4) Guselkumab 100 mg: −10.8 (7.3) Guselkumab 200 mg: −11.4 (6.8)		
Griffiths et al., 2010[51] None Moderate	Ustekinumab 45 mg or 90 mg at weeks 0 and 4 etanercept 50 mg twice weekly	Ustekinumab 45mg: 209 Ustekinumab 90 mg: 347 Etanercept 50 mg: 347	*Primary outcomes at week 12* **% PASI 75** 56.8% (etanercept) vs. 67.5% (ustekinumab 45 mg); *P* = .01 56.8% (etanercept) vs. 73.8% (ustekinumab 90 mg); *P* < .001 *Secondary outcomes at week 12* **% PASI 90** 23.1% (etanercept) vs. 36.4% (ustekinumab 45 mg); *P* < .001	**N (%) AE** Etanercept: 243 (70) Ustekinumab 45 mg: 138 (66) Ustekinumab 90 mg: 240 (69.2) RR, 1.03; 95% CI, 0.94 to 1.13 for etanercept vs. ustekinumab (combined dosages)	**N (%) 1 infection** Etanercept: 101 (29.1) Ustekinumab 45 mg: 64 (30.6) Ustekinumab 90 mg: 103 (29.7) **N (%) injection-site reaction**

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			23.1% (etanercept) vs. 44.7% (ustekinumab 90 mg); *P* = .01 **% PGA 0 or 1** 49.0% (etanercept) vs. 65.1% (ustekinumab 45 mg); *P* < .001 49.0% (etanercept) vs. 70.6% (ustekinumab 90 mg); *P* < .001 **% PGA 0** 8.6% (etanercept) vs. 16.3% (ustekinumab 45 mg); *P* = .006 8.6% (etanercept) vs. 26.2% (ustekinumab 90 mg); *P* < .001	**N (%) SAE** Etanercept: 4 (1.2) Ustekinumab 45 mg: 4 (1.9) Ustekinumab 90 mg: 4 (1.2) RR, 0.80; 95% CI, 0.35 to 2.77 for etanercept vs. ustekinumab **N (%) withdrawal due to AE** Etanercept: 8 (2.3) Ustekinumab 45 mg: 4 (1.9) Ustekinumab 90 mg: 4 (1.2) Calculated RR, 1.6; 95% CI, 0.61 to 4.23 for etanercept vs. ustekinumab	Etanercept: 86 (24.8) Ustekinumab 45 mg: 9 (4.3) Ustekinumab 90 mg: 13 (3.7) RR, 6.26; 95% CI, 4.0 to 9.81 for etanercept vs. ustekinumab, however, participants in etanercept group received more injections than those in the ustekinumab groups.
Griffiths et al., 2015[68] UNCOVER-2 UNCOVER-3 Moderate	UNCOVER-2 Ixekizumab 80 mg every 2 weeks[a] Ixekizumab 80 mg every 4 weeks[a] Etanercept 50 mg twice weekly Placebo (n = 168) UNCOVER-3 Ixekizumab 80 mg every 2 weeks[a]	UNCOVER-2 Ixekizumab 2-wk: 351 Ixekizumab 4-wk: 347 Etanercept: 358 Placebo: 168 UNCOVER-3 Ixekizumab 2-wk: 385 Ixekizumab 4-wk: 386 Etanercept: 382	*Primary outcomes at week 12* **% PASI 75** U2: 89.7% (ixekizumab 2-wk) vs. 77.5% (ixekizumab 4-wk) vs. 41.6% (etanercept); effect size ixekizumab 2-wk vs. etanercept: 48.1%; (97.5% CI: 41.2% to 55.0%); effect size ixekizumab 4wk vs. etanercept: 35.9% (97.5% CI, 28.2% to 43.6%) U3: 87.3% (ixekizumab 2-wk) vs. 84.2% (ixekizumab 4-wk) vs. 53.4% (etanercept); effect size ixekizumab 4-wk vs. etanercept: 30.8% (97.5% CI, 23.7% to 37.9%), effect size ixekizumab 2-wk vs. etanercept: 33·9% (97.5% CI, 27.0% to 40.7%) **% PGA 0 or 1**	*AEs for UNCOVER-2 and UNCOVER-3 were pooled by study authors* **% (N) Any TEAE** Ixekizumab 2-wk: 58% (424/734) Ixekizumab 4-wk: 58% (419/729) Etanercept: 54% (399/739) **% (N) Nonfatal SAE** Ixekizumab 2-wk: 1.9% (14/734) Ixekizumab 4-wk: 1.9% (14/729)	*AEs for UNCOVER-2 and UNCOVER-3 were pooled by study authors* **% (N) Injection-site reactions** Ixekizumab 2-wk: 10% (76/734) Ixekizumab 4-wk: 9% (62/729) Etanercept: 11% (80/739) The most

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	Ixekizumab 80 mg every 4 weeks[a] Etanercept 50 mg twice weekly Placebo	Placebo: 193	U2: 83.2% (ixekizumab 2-wk) vs. 72.9% (ixekizumab 4-wk) vs. 36.0% (etanercept) U3: 80.5% (ixekizumab 2-wk) vs. 75.4% (ixekizumab 4-wk) vs. 41.6% (etanercept), Ixekizumab 2-wk vs. etanercept effect size U2: 47.2% (97.5% CI, 39.9% to 54.4%); U3: 38.9% (97.5% CI, 31.7% to 46.1%) Ixekizumab 4-wk vs. etanercept effect size U 2: 36.9% (97.5% CI, 29.1% to 44.7%); U3: 33.8% (97.5% CI, 26.3% to 41.3%) *Secondary outcomes* **% PGA 0** U2: 42% vs. 32% vs. 6%, effect size ixekizumab 4-wk vs. etanercept: 26.4% (97.5% CI, 20.1% to 32.7%); effect size ixekizumab 2-wk vs. etanercept: 36.0% (97.5% CI, 29.5% to 42.5%) U3: 40% vs. 36% vs. 9%, effect size ixekizumab 4-wk vs. etanercept: 27.4% (97.5% CI, 21.0% to 33.7%); effect size ixekizumab 2-wk vs. etanercept: 31.6% (97.5% CI, 25.2% to 38.1%) **% PASI 90** U2: 71% vs. 60% vs. 19%, effect size ixekizumab 4-wk vs. etanercept: 40.9% (97.5% CI, 33.4% to 48.4%); ixekizumab 2-wk vs. etanercept: 51.9% (97.5% CI, 44.8% to 59.1%) U3: 68% vs. 65% vs. 26%, effect size ixekizumab 4-wk vs. etanercept: 39.6% (97.5% CI, 32.2% to 47.0%); ixekizumab 2- wk. vs. etanercept: 42.4% (97.5% CI, 35.1% to 49.7%) **% PASI 100** U2: 41% vs. 31% vs. 5%, effect size ixekizumab 4-wk vs. etanercept: 25.5% (97.5% CI, 19.4% to 31.7%); effect size ixekizumab 2-wk vs. etanercept: 35.1% (97.5% CI, 28.7% to 41.6%) U3: 38% vs. 35% vs. 7%, effect size ixekizumab	Etanercept: 2% (15/739) **% (N) Withdrawal due to AE** Ixekizumab 2-wk: 1.6% (12/736) Ixekizumab 4-wk: 1.9% (14/733) Etanercept: 1.2% (9/740)	common AEs (≥2% of all participants given ixekizumab): nasopharyngitis, upper respiratory tract infection, injection-site reaction, injection-site erythema, injection-site pain, pruritus, headache, and arthralgia. Most treatment-emergent AEs were mild or moderate in severity. No deaths.

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			4-wk vs. etanercept: 27.6% (97.5% CI, 21.4% to 33.9%) **Itch NRS** % of participants with a 4-point improvement from baseline U2: 85% vs. 77% vs. 58% U3: 83% vs. 80% vs. 64% **% DLQI 0 or 1** U2: 64% vs. 60% vs. 34%; effect size ixekizumab 2-wk vs. etanercept: 30.3% (97.5% CI, 22.3% to 38.3%); effect size ixekizumab 4-wk vs. etanercept: 26.1% (97.5% CI, 18.0% to 34.3%); U3: 65% vs. 64% vs. 44%; effect size ixekizumab 4-wk vs. etanercept: 20.0% (97.5% CI, 12.1% to 27.9%); effect size ixekizumab 2-wk vs. etanercept: 21.0% (97.5% CI, 13.1% to 28.8%).		
Langley et al., 2014[45] FIXTURE Moderate	Secukinumab 300 mg weekly (induction of 4 weeks) then every 4 weeks Secukinumab 150 mg weekly (induction of 4 weeks) then every 4 weeks Etanercept 50 mg (twice weekly 1-12 weeks, then once weekly through week 51) Placebo	Secukinumab 300 mg: 327 Secukinumab 150 mg: 327 Etanercept: 326 Placebo: 326 Total: 1,306	*Primary study endpoints were all efficacy of secukinumab vs. placebo outcomes.* *Key comparative effectiveness outcomes (secondary study endpoints)* **% PASI 75 at week 12** 77.1% (secukinumab 300 mg) vs. 67.0% (secukinumab 150 mg) vs. 44.0% (etanercept 50 mg) *P* < .001 for both doses secukinumab vs. etanercept **% PGA 0 or 1 at week12** 62.5% (secukinumab 300 mg) vs. 51.1% (secukinumab 150 mg) vs. 27.2% (etanercept 50 mg) *P* < .001 for both doses secukinumab vs. etanercept *Other secondary outcomes* **% PASI 90 at week 12** 54.2% (secukinumab 300 mg) vs. 41.9% (secukinumab 150 mg) vs. 20.7% (etanercept 50	**% (N) AE** Secukinumab 300 mg: 81% (376 of 467); 252 events per 100 patient-years Secukinumab 150 mg: 78% (364 of 469); 236 events per 100 patient-years Etanercept: 78% (253 of 323); 234 events per 100 patient-years **% (N) nonfatal SAE** Secukinumab 300 mg: 6% (27 of 467); 7 events per 100 patient-years Secukinumab 150 mg: 5% (24 of 469); 6 events per 100	**% (N) injection-site reaction** Combined Secukinumab groups: 1% (7 of 936) Etanercept: 11% (36 of 323)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			mg) *P* < .001 for both doses secukinumab vs. etanercept **% PASI 75 response at week 12 that continued to have response at week 52** 84.3% (secukinumab 300 mg) vs. 82.2% (secukinumab 150 mg) vs. 72.5% (etanercept 50 mg) *P* < .001 for 300 mg vs. etanercept; *P* = .009 for 150 mg vs. etanercept **% PGA 0 or 1 response at week 12 that continued to have response at week 52** 79.7% (secukinumab 300 mg) vs. 67.7% (secukinumab 150 mg) vs. 56.8% (etanercept 50 mg) *P* < .001 for 300 mg vs. etanercept; *P* = .002 for 150 mg vs. etanercept **% PASI 100 at week 12** 24.1% (secukinumab 300 mg) vs. 14.4% (secukinumab 150 mg) vs. 4.3% (etanercept 50 mg) *P* < .001 for both doses secukinumab vs. etanercept **DLQI change in mean score at 12 weeks** −10.4 (secukinumab 300 mg) −9.7 (secukinumab 150 mg) −7.9 (etanercept 50 mg) (No *P* reported)	patient-years Etanercept: 6% (20 of 323); 7 events per 100 patient-years **% (N) withdrawal due to AE** Secukinumab 300 mg: 3% (14 of 467) Secukinumab 150 mg: 2% (10 of 469) Etanercept: 4% (12 of 323)	
Lebwohl et al., 2018[15] CIMPACT Moderate	Certolizumab pegol 200 mg SC (after 400 mg loading doses at weeks 0, 2, and 4) for 16 weeks Certolizumab	Certolizumab pegol 200 mg: 165 Certolizumab pegol 400 mg: 167 Etanercept:	At 12 weeks N (%) PASI 75 Certolizumab pegol 200 mg: 101 (61.3) Certolizumab pegol 400 mg: 111 (66.7) Etanercept: 91 (53.3) Reported ARD (95% CI) Certolizumab pegol 200 mg vs. etanercept: 8.0 (–	N (%) [incidence rate as cases per 100 patient-years] Any TEAE Certolizumab pegol 200 mg: 78 (47.3) [299.5]	N (%) [incidence rate as cases per 100 patient-years] infections and infestations Certolizumab pegol 200 mg:

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	pegol 400 mg SC every 2 weeks for 16 weeks Etanercept 50 mg SC twice weekly for 12 weeks (the final 4 weeks were considered a washout period)	170 Total: 502	2.9 to 18.9) Reported OR (95% CI): 1.4 (0.9 to 2.2), *P* = .15 Calculated RR (95% CI): 1.1 (0.95 to 1.4), *P* = .16 Certolizumab pegol 400 mg vs. etanercept Reported ARD (95% CI) 13.4 (2.7 to 24.1) Reported OR (95%): 1.8 (1.1 to 2.8), *P* = .02 Calculated RR: 1.2 (1.04 to 1.5), *P* = .02 N (%) PASI 90 Certolizumab pegol 200 mg: 51 (31.2) Certolizumab pegol 400 mg: 57 (34.0) Etanercept: 46 (27.1) Certolizumab 200 mg vs. etanercept Calculated ARD (95% CI): 3.9 (–5.9 to 13.6), *P* = .44 Calculated RR (95% CI): 1.1 (0.82 to 1.6) Certolizumab 400 mg vs. etanercept Calculated ARD (95% CI): 7.1 (–2.7 to 16.9), *P* = .16 Calculated RR (95% CI): 1.3 (0.91 to 1.7) % PGA 0 or 1 Certolizumab pegol 200 mg: 66 (39.8) Certolizumab pegol 400 mg: 84 (50.3) Etanercept: 67 (39.2) Certolizumab 200 mg vs. etanercept Calculated ARD (95% CI): 0.59 (–9.9 to 11.1), *P* = .91 Calculated RR (95% CI): 1.02 (0.78 to 1.3) Certolizumab 400 mg vs. etanercept Calculated ARD (95% CI): 10.9 (0.33 to 21.4), *P* = .045 Calculated RR (95% CI): 1.3 (1.004 to 1.6)	Certolizumab pegol 400 mg: 82 (49.1) [309.2] Etanercept: 78 (46.4) [295.6] 200 mg vs. etanercept Calculated RR, 1.02, 95% CI, 0.81 to 1.3 400 mg vs. etanercept Calculated RR, 1.06, 95% CI, 0.85 to 1.3 N (%) serious [incidence rate as cases per 100 patient-years] TEAE Certolizumab pegol 200 mg: 1 (0.6) [2.7] Certolizumab pegol 400 mg: 4 (2.4) [10.6] Etanercept: 1 (0.6) [2.7] 200 mg vs. etanercept Calculated RR, 1.02, 95% CI, 0.06 to to 16.1 400 mg vs. etanercept Calculated RR, 4.0, 95% CI, 0.45 to 35.6 N (%) discontinuations due to TEAE Certolizumab pegol 200 mg: 1 (0.6) Certolizumab pegol 400 mg: 1 (0.6) Etanercept: 4 (2.4)	44 (26.7) [134.9] Certolizumab pegol 400 mg: 38 (22.8) [113.1] Etanercept: 39 (23.2) [120.0] Of these, only 1 (in certolizumab 400 mg group) was considered serious. Malignancy 0 in all groups Mortality 0 in all groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
				200 mg vs. etanercept Calculated RR, 0.25, 95% CI, 0.03 to 2.3 400 mg vs. etanercept Calculated RR, 0.25, 95% CI, 0.03 to 2.2	
Lebwohl et al., 2015[37] Hsu et al., 2020[76] Lambert et al., 2021[82] Warren et al., 2021[81] AMAGINE-2 AMAGINE-3 Moderate	Brodalumab 210 mg SC on day 1, weeks 1, 2, 4, 6, 8, 10 Brodalumab 140 mg SC on day 1, week 1, then every 2 weeks Ustekinumab 45 mg subcutaneous for participants with a body weight ≤100 kg and 90 mg for participants >100 kg on day 1 and week 4 Placebo Induction phase: 12 weeks Maintenance phase: 40 weeks Pooled analyses used data from participants who received continuous brodalumab 210	Brodalumab 210 mg A2: 612 A3:624 Brodalumab 140 mg A2: 610 A3: 629 Ustekinumab A2:300 A3: 313 Placebo A2: 309 A3: 315 A2 and A3 pooled analyses Brodalumab 210 mg: 339 Ustekinumab: 590	*Primary outcome for comparative effectiveness at 12 weeks* **% PASI 100** A2: Brodalumab 210 mg: 44%, Ustekinumab: 22%, *P* < .001 A3: Brodalumab 210 mg 37%, Ustekinumab: 19% *P* < .001 *Key secondary outcome for comparative effectiveness at 12 weeks* **% PASI 75** A2: Brodalumab 210 mg: 86%, Ustekinumab: 70%, *P* = .08 A3: Brodalumab 210 mg: 85%, Ustekinumab: 69%, *P* = .007 *Other secondary outcomes at 12 weeks* **% PGA 0 or 1** A2: Brodalumab: 79 Ustekinumab: 61, *P* < .001 A3: brodalumab:80 ustekinumab: 57, *P* < .001 **% PGA 0** A2: Brodalumab: 45 Ustekinumab: 22, *P* < .001 A3: Brodalumab 37 Ustekinumab: 19, *P* < .001 **% DLQI 0 or 1** A2 and A3 pooled Brodalumab: 59.5	*At 12 weeks* **% (N) AE** A2: Brodalumab 210 mg: 57.8 (354) Ustekinumab: 59, (177) A3: Brodalumab 210 mg: 56.8 (353) Ustekinumab: 53.7 (168) **% (N) SAE** A2: Brodalumab 210 mg: 1.0 (6) Ustekinumab: 1.3 (4) A3: Brodalumab 210 mg: 1.4 (9) Ustekinumab: 0.6 (2) **% (N) discontinued study due to AE** A2: Brodalumab 210 mg: 1.0 (6) Ustekinumab: 0.7 (2) A3: Brodalumab 210 mg: 0.8 (5) Ustekinumab: 0.3 (1) **% (N) discontinued drug due to AE** A2: Brodalumab 210 mg: 1.0 (6)	One death (from stroke) occurred during the induction phase (in the AMAGINE-2 study, in a patient in the 210 mg brodalumab group, 20 days after the last dose)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	mg or ustekinumab for the full 52-week study period		Ustekinumab: 45.6 OR, 1.74; 95% CI, 1.32 to 2.31 *Outcomes at 52 weeks* A2 and A3 pooled **% PASI 100** Brodalumab: 51 Ustekinumab: 28 OR, 2.8; 95% CI, 2.1 to 3.7 **% PASI 90** Brodalumab : 63.1 Ustekinumab: 42.7 OR, 2.5; 95% CI, 1.9 to 3.4 **% DLQI 0 or 1** Brodalumab: 54.9 Ustekinumab: 39.8 OR, 1.90, 95% CI, 1.43 to 2.53 *Subgroup analysis (A2 and A3 pooled)* Comparable efficacy between participants with BMI < 30 kg/m^2 and those > 30 kg/m^2	Ustekinumab: 1.3 (4) A3: Brodalumab 210 mg: 1.1 (7) Ustekinumab: 0.6 (2) *Subgroup analysis (A2 and A3 pooled)* Comparable safety between participants with BMI < 30 kg/m^2 and those > 30 kg/m^2	
McInnes et al., 2021[26] SELECT-PsA 1 Moderate	Upadacitinib 15 mg oral once daily for 24 weeks Upadacitinib 30 mg oral once daily for 24 weeks Adalimumab 40 mg SC every other week for 24 weeks Placebo through week 24 then this group was	Upadacitinib 15 mg: 429 Upadacitinib 30 mg: 423 Adalimumab: 429 Total: 1281 included in this update Placebo: 423 (not included in this update)	All comparisons vs. adalimumab were secondary outcomes At 12 weeks N (%) ACR 20 (superiority analyses) Upadacitinib 15 mg: 303 (70.6) Upadacitinib 30 mg: 332 (78.5) Adalimumab: 279 (65) Upadacitinib 15 mg vs. adalimumab Reported ARD (95% CI): 5.6 (–0.65 to 11.80), *P* = .08 Calculated RR (95% CI): 1.1 (0.99 to 1.2) Upadacitinib 30 mg vs. adalimumab Reported ARD (95% CI): 13.5 (7.5 to 19.4), *P* < .001 Calculated RR (95% CI): 1.2 (1.1 to 1.3)	N (%) any AE Upadacitinib 15 mg: 287 (66.9) Upadacitinib 30 mg: 306 (72.3) Adalimumab: 278 (64.8) Calculated RR (95% CI) vs. adalimumab Upadacitinib 15 mg: 1.03 (0.94 to 1.1) Upadacitinib 30 mg: 1.1 (1.02 to 1.2) N (%) serious AE Upadacitinib 15 mg:	N (%) infections Upadacitinib 15 mg: 169 (39.4) Upadacitinib 30 mg: 183 (43.3) Adalimumab: 146 (34.0) N (%) serious infections Upadacitinib 15 mg: 5 (1.2) Upadacitinib 30 mg: 11 (2.6) Adalimumab: 3 (0.7)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	rerandomized to upadacitinib 15 mg or 30 mg Starting at week 16, participants who did not have at least a 20% improvement could initiate background treatment with DMARDs, NSAIDs, acetaminophen, opioids, glucocorticoids or adjust drugs they were already taking		ACR20 noninferiority analysis, Percentage of adalimumab effect preserved (95% CI) Upadacitinib 15 mg vs. adalimumab: 119.4 (98.0 to 147.9); *P* < .001 Upadacitinib 30 mg vs. Adalimumab: 146.6 (122.8 to 180.4); *P* < .001 N (%) ACR50 Upadacitinib 15 mg: 161 (37.5) Upadacitinib 30 mg: 219 (51.8) Adalimumab: 161 (37.5) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 0.0 (−6.5 to 6.5), *P* = 1.0 Calculated RR (95% CI): 1.0 (0.84 to 1.20) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 14.2 (7.6 to 20.9), *P* < .001 Calculated RR (95% CI): 1.4 (1.2 to 1.6) N (%) ACR70 Upadacitinib 15 mg: 67 (15.6) Upadacitinib 30 mg: 107 (25.3) Adalimumab: 59 (13.8) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 1.9 (−2.9 to 6.6), *P* = .44 Calculated RR (95% CI): 1.1 (0.82 to 1.6) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 11.5 (6.3 to 16.8), *P* < .001 Calculated RR (95% CI): 1.8 (1.4 to 2.5) Mean change (95% CI) in HAQ-DI Upadacitinib 15 mg: −0.42 (−0.47 to −0.37) Upadacitinib 30 mg: −0.47 (−0.52 to −0.42) Adalimumab: −0.34 (−0.38 to −0.29) Mean difference in change (95% CI)	14 (3.3) Upadacitinib 30 mg: 26 (6.1) Adalimumab: 16 (3.7) Calculated RR (95% CI) vs. adalimumab Upadacitinib1 5 mg: 0.88 (0.43 to 1.8) Upadacitinib 30 mg: 1.6 (0.90 to 3.0) N (%) discontinuations due to AE Upadacitinib 15 mg: 13 (3.0) Upadacitinib 30 mg: 21 (5.0) Adalimumab: 22 (5.1) Calculated RR (95% CI) vs. adalimumab Upadacitinib 15 mg: 0.59 (0.30 to 1.2) Upadacitinib 30 mg: 0.97 (0.54 to 1.7)	Mortality 0 in all groups N (%) cancer Upadacitinib 15 mg: 1 (0.2) Upadacitinib 30 mg: 3 (0.7) Adalimumab: 3 (0.7) N (%) cancer other than nonmelanoma skin cancer Upadacitinib 15 mg: 1 (0.2) Upadacitinib 30 mg: 1 (0.2) Adalimumab: 3 (0.7) N (%) major adverse cardiovascular event Upadacitinib 15 mg: 0 (0) Upadacitinib 30 mg: 0 (0) Adalimumab: 2 (0.5)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Upadacitinib 15 mg vs. Adalimumab: −0.08 (−0.15 to −0.01) Upadacitinib 30 mg vs. Adalimumab: −0.14 (−0.20 to −0.07) Mean change (95% CI) change in patient assessment of pain Upadacitinib 15 mg: −2.3 (−2.5 to −2.0) Upadacitinib 30 mg: −2.7 (−2.9 to −2.5) Adalimumab: −2.3 (−2.5 to −2.1) Mean difference in change (95% CI) Upadacitinib 15 mg vs. adalimumab: −0.0 (−0.3 to 0.3) Upadacitinib 30 mg vs. adalimumab: −0.5 (−0.7 to −0.2) Mean change (95% CI) in SF-36 PCS Upadacitinib 15 mg: 7.9 (7.1 to 8.6) Upadacitinib 30 mg: 8.9 (8.1 to 9.7) Adalimumab: 6.8 (6.1 to 7.6) Mean difference in change (95% CI) Upadacitinib 15 mg vs. Adalimumab: Upadacitinib 30 mg vs. Adalimumab: Mean change (95% CI) in FACIT-F Upadacitinib 15 mg: 6.3 (5.4 to 7.2) Upadacitinib 30 mg: 7.1 (6.2 to 8.0) Adalimumab: 5.7 (4.8 to 6.6) Mean difference in change (95% CI) Upadacitinib 15 mg vs. adalimumab: Upadacitinib 30 mg vs. adalimumab: At 16 weeks N (%) sIGA of Psoriasis 0 or 1 and ≥ 2 point decrease from baseline Upadacitinib 15 mg: 135 (41.9) Upadacitinib 30 mg: 175 (54)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Adalimumab: 127 (38.5) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 3.4 (−4.1 to 11.0), *P* = .37 Calculated RR (95% CI): 1.1 (0.90 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 15.5 (8.0 to 23.1), *P* < .001 Calculated RR (95% CI): 1.4 (1.2 to 1.7) N (%) PASI 75 Upadacitinib 15 mg: 134 (62.6) Upadacitinib 30 mg: 131 (62.4) Adalimumab: 112 (53.1) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 9.5 (0.19 to 18.9); *P* = .047 Calculated RR (95% CI): 1.2 (1.001 to 1.4) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 9.3 (−0.09 to 18.70); *P* = .05 Calculated RR (95% CI): 1.2 (0.99 to 1.4) N (%) PASI 90 Upadacitinib 15 mg: 83 (38.9) Upadacitinib 30 mg: 104 (49.5) Adalimumab: 81 (38.3) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 0.40 (−8.9 to 9.7), *P* = .93 Calculated RR (95% CI): 1.01 (0.79 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 11.1 (1.7 to 20.6); *P* = .02 Calculated RR (95% CI): 1.3 (1.04 to 1.6) N (%) PASI 100 Upadacitinib 15 mg: 51 (23.8)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Upadacitinib 30 mg: 71 (33.8) Adalimumab: 42 (19.9) Upadacitinib 15 mg vs. adalimumab Calculated ARD: 3.9 (−3.9 to 11.8), *P* = .33 Calculated RR (95% CI): 1.2 (0.83 to 1.7) Upadacitinib 30 mg vs. Adalimumab Calculated ARD (95% CI): 13.9 (5.5 to 22.3), *P* = .001 Calculated RR (95% CI): 1.7 (1.2 to 2.4) Mean change (95% CI) in Self-Assessment of Psoriasis Symptoms score Upadacitinib 15 mg: −25.3 (−27.3 to −23.4) Upadacitinib 30 mg: −28.1 (−30 to −26.1) Adalimumab: −22.7 (−24.7 to −20.8) Mean difference in change (95% CI) Upadacitinib 15 mg vs. Adalimumab: Upadacitinib 30 mg vs. Adalimumab: At 24 weeks N (%) MDA Upadacitinib 15 mg: 157 (36.6) Upadacitinib 30 mg: 192 (45.4) Adalimumab: 143 (33.3) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 3.3 (−3.1 to 9.6), *P* = .32 Calculated RR (95% CI): 1.1 (0.91 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 12.1 (5.5 to 18.6); *P* < .001 Calculated RR (95% CI): 1.4 (1.1 to 1.6) N (5) achieving sIGA 0 or 1 Upadacitinib 15 mg: 146 (45.3) Upadacitinib 30 mg: 170 (52.5) Adalimumab: 134 (40.6)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI):4.7 (−2.9 to 12.3); *P* = .22 Calculated RR (95% CI): 1.1 (0.94 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 11.9 (4.3 to 19.5); *P* = .002 Calculated RR (95% CI): 1.3 (1.1 to 1.5) N (%) resolution of enthesitis (LEI = 0) Upadacitinib 15 mg: 145 (53.7) Upadacitinib 30 mg: 154 (57.7) Adalimumab: 125 (47.2) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 6.5 (−1.9 to 15.0); *P* = .13 Calculated RR (95% CI): 1.1 (0.96 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 10.5 (2.1 to 19.0); *P* = .02 Calculated RR (95% CI): 1.2 (1.04 to 1.4) N (%) resolution of enthesitis (SPARCC Enthesitis Index = 0) Upadacitinib 15 mg; 156 (47.6) Upadacitinib 30 mg: 173 (53.2) Adalimumab: 138 (43.0) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 4.6 (−3.1 to 12.2); *P* = .24 Calculated RR (95% CI): 1.1 (0.93 to 1.3) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 10.2 (2.6 to 17.9); *P* = .009 Calculated RR (95% CI): 1.2 (1.1 to 1.5) N (%) resolution of dactylitis (LDI = 0) Upadacitinib 15 mg: 104 (76.5)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Upadacitinib 30 mg: 101 (79.5) Adalimumab: 94 (74) Upadacitinib 15 mg vs. adalimumab Calculated ARD (95% CI): 2.5 (–8.0 to 12.9); *P* = .65 Calculated RR (95% CI): 1.03 (0.90 to 1.2) Upadacitinib 30 mg vs. adalimumab Calculated ARD (95% CI): 5.5 (–4.9 to 15.9), *P* = .30 Calculated RR (95% CI): 1.07 (0.94 to 1.2)		
McInnes et al., 2020[16] Gottlieb et al., 2021[35] EXCEED Moderate	Secukinumab 300 mg SC at baseline, weeks 1, 2, 3, and 4 and then every 4 weeks until week 48 Adalimumab 40 mg SC every 2 weeks until week 50 Placebo injections used to maintain blinding	Secukinumab: 426 Adalimumab: 427 Total: 853	At 52 weeks (ORs adjusted for baseline weight; participants discontinuing treatment prematurely or who took csDMARDs after week 36 were considered nonresponders) N (%) ACR20 Secukinumab: 285 (67) Adalimumab: 265 (62) Reported OR (95% CI): 1.3 (0.98 to 1.7), *P* = .07 Calculated RR (95% CI): 1.1 (0.98 to 1.2), *P* = .14 N (%) ACR20 (prespecified sensitivity analysis with missing values imputed) Secukinumab: 285 (67) Adalimumab: 254 (59) Reported OR (95% CI): 1.38 (1.04 to 1.83), *P* = .02 Calculated RR (95% CI): 1.1 (1.02 to 1.2), *P* = .03 N (%) PASI 90 Secukinumab: 277 (65) Adalimumab: 184 (43) Reported OR (95% CI): 2.5 (1.7 to 3.7), *P* < .0001 Calculated RR (95% CI): 1.5 (1.3 to 1.7), *P* < .0001 N (%) ACR50 Secukinumab: 209 (49) Adalimumab: 192 (45) Reported OR (95% CI): 1.2 (0.90 to 1.6), *P* = .23	N (%) any AE Secukinumab: 330 (77) Adalimumab: 338 (79) Calculated RR (95% CI): 0.98 (0.91 to 1.10) N (%) nonfatal SAE Secukinumab: 32 (8) Adalimumab: 28 (7) Calculated RR (95% CI): 1.1 (0.70 to 1.90) N (%) withdrawals due to AE Secukinumab: 17 (4) Adalimumab: 32 (7) Calculated RR (95% CI): 0.53 (0.30 to 0.94)	N (%) infections and infestations Secukinumab: 237 (56) Adalimumab: 234 (55) N (%) serious infections Secukinumab: 7 (2) Adalimumab: 6 (1) N (%) injection-site reactions Secukinumab: 17 (4) Adalimumab: 47 (11) Major adverse cardiac event Secukinumab: 2 (0.47) Adalimumab: 0 (0) N (%) mortality

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Calculated RR (95% CI): 1.1 (0.95 to 1.3), *P* = .23 Mean (SE) change HAQ-DI score Secukinumab: −0.58 (0.03) (n = 363) Adalimumab: −0.56 (0.03) (n = 318) Between-group mean difference (95% CI): −0.02 (−0.10 to 0.05), *P* = .55 N (%) resolution of enthesitis based on LEI Secukinumab: 260 (61) Adalimumab: 231 (54) Reported OR (95% CI): 1.3 (0.91 to 1.9), *P* = .15 Calculated RR (95% CI): 1.1 (1.005 to 1.3), *P* = .04 Twelve other exploratory psoriatic arthritis endpoints reported, all but 3 reported no significant differences between groups. Three other exploratory skin endpoints reported, all were consistent with the PASI 90 findings. Two other exploratory QoL endpoints reported, all were consistent with the HAQ-DI mean change score findings. Similar findings among subgroup of participants with moderate-to-severe psoriasis.		Secukinumab: 1 (0,23) Adalimumab: 0 (0)
Mease et al., 2020[18] Smolen et al., 2020[33] Smolen et al., 2020[34] SPIRIT-H2H Moderate	Ixekizumab 160 mg SC starting dose at week 0 then 80 mg SC every 4 weeks from week 4 onward until week 24 or if had moderate-to-severe psoriasis then 80 mg SC every 2 weeks from week 2 to week 12 then	Ixekizumab: 283 Adalimumab: 283 Total: 566	Primary outcome At 24 weeks N (%) ACR50 and PASI100 Ixekizumab: 102 (36.0) Adalimumab: 79 (27.9) Reported ARD (95% CI): 8.1 (0.5 to 15.8) Calculated RR (95% CI): 1.3 (1.01 to 1.6) Secondary outcomes At 24 weeks N (%) PASI 100 Ixekizumab: 170 (60.1) Adalimumab: 132 (46.6) Reported ARD (95% CI): 13.4 (5.3 to 21.6) Calculated RR (95% CI): 1.3 (1.1 to 1.5)	At 52 weeks N (%) any TEAE Ixekizumab: 209 (73.9) Adalimumab: 194 (68.6) Calculated RR (95% CI): 1.1 (0.97 to 1.2) N (%) serious AE Ixekizumab: 12 (4.2) Adalimumab: 35 (12.4) Calculated RR (95% CI): 0.34 (0.18 to 0.65) N (%) discontinuations due to AE	At 52 weeks N (%) infections Ixekizumab: 119 (42) Adalimumab: 111 (39.2) N (%) serious infections Ixekizumab: 5 (1.8) Adalimumab: 8 (2.8) N (%) cerebrocardiova

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	every 4 weeks until week 24 Adalimumab 40 mg SC starting dose then 40 mg SC every 2 weeks starting at week 2 until week 24 or if had moderate-to-severe psoriasis then 80 mg SC starting dose at week 0 then at week 1 40 mg SC every 2 weeks until week 24		N (%) ACR50 Ixekizumab: 143 (50.5) Adalimumab: 132 (46.6) Reported ARD (95% CI): 3.9 (−4.3 to 12.1) Calculated RR (95% CI): 1.1 (0.91 to 1.3) Noninferiority analysis (prespecificed margin for the lower bound of 95% CI was −12%): treatment difference (95% CI), 3.9% (−4.3% to 12.1%) N (%) ACR20 Ixekizumab: 195 (68.9) Adalimumab: 204 (72.1) Reported ARD (95% CI): −3.2 (−10.7 to 4.3) Calculated RR (95% CI): 0.96 (0.86 to 1.1) N (%) ACR70 Ixekizumab: 90 (31.8) Adalimumab: 73 (25.8) Reported ARD (95% CI): 6.0 (−1.4 to 13.5) Calculated RR (95% CI): 1.2 (0.95 to 1.6) N (%) MDA Ixekizumab: 135 (47.7) Adalimumab: 100 (35.3) Reported ARD (95% CI): 12.4 (4.3 to 20.4) Calculated RR (95% CI): 1.4 (1.1 to 1.6) Mean change (SE) from baseline in mCPDAI Ixekizumab: −3.9 (0.14) Adalimumab: −3.5 (0.13) Mean difference: −0.53 (−0.85 to −0.20) N (%) SPARCC Enthesitis Index = 0 (among those with score > 0 at baseline) Ixekizumab: 107/189 (56.6) Adalimumab: 77/171 (45) Reported ARD (95% CI): 11.6 (1.3 to 21.9) Calculated RR (95% CI): 1.3 (1.02 to 1.5) N (%) LEI Enthesitis Index = 0 (among those with	Ixekizumab: 12 (4.2) Adalimumab: 21 (7.4) Calculated RR (95% CI): 0.57 (0.29 to 1.1)	scular events Ixekizumab: 5 (1.8) Adalimumab: 7 (2.5) N (%) malignancies Ixekizumab: 0 (0) Adalimumab: 4 (1.4) N (%) injection-site reactions Ixekizumab: 30 (10.6) Adalimumab: 10 (3.5) Calculated RR (95% CI): 3.0 (1.5 to 6.0) Mortality 0 in all groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			score >0 at baseline) Ixekizumab: 95/159 (59.7) Adalimumab: 81/147 (55.1) Reported ARD (95% CI): 4.6 (−6.4 to 15.7) Calculated RR (95% CI): 1.1 (0.89 to 1.3) N (%) LDI-B Leeds Dactylitis Index = 0 (among those with score > 0 at baseline) Ixekizumab: 37/42 (88.1) Adalimumab: 54/58 (93.1) Reported ARD (95% CI): −5.0 (−16.8 to 6.8) Calculated RR (95% CI): 0.95 (0.83 to 1.1) N (%) PASI 75 Ixekizumab: 227 (80.2) Adalimumab: 195 (68.9) Reported ARD (95% CI): 11.3 (4.2 to 18.4) Calculated RR (95% CI): 1.2 (1.06 to 1.3) N (%) PASI 90 Ixekizumab: 203 (71.7) Adalimumab: 158 (55.8) Reported ARD (95% CI): 15.9 (8.1 to 23.7) Calculated RR (95% CI): 1.3 (1.1 to 1.5) N (%) NAPSI fingernails = 0 (among those with score > 0 at baseline) Ixekizumab: 111/191 (58.1) Adalimumab: 88/177 (49.7) Reported ARD (95% CI): 8.4 (−1.8 to 18.6) Calculated RR (95% CI): 1.2 (0.97 to 1.4) Mean change (SE) from baseline in NAPSI Ixekizumab: −15.9 (0.82) Adalimumab: −12.5 (0.82) Reported mean difference: −3.4 (−5.4 to −1.3) N (%) ≥ 0.35 point improvement from baseline in HAQ-DI (among those with score > 0.35 at baseline)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Ixekizumab: 168/252 (66.7) Adalimumab: 166/254 (65.4) Reported ARD (95% CI): 1.3 (−6.9 to 9.6) Calculated RR (95% CI): 1.02 (0.90 to 1.2) N (%) DLQI 0 or 1 Ixekizumab: 174 (61.5) Adalimumab: 147 (51.9) Reported ARD (95% CI): 9.5 (1.4 to 17.7) Calculated RR (95% CI): 1.2 (1.02 to 1.4) At 52 weeks N (%) ACR50 and PASI100 Ixekizumab: 111 (39.2) Adalimumab: 74 (26.1) Reported ARD (95% CI): 13.1 (5.4 to 20.7) Calculated RR (95% CI): 1.5 (1.2 to 1.9) N (%) ACR50 Ixekizumab: 141 (49.8) Adalimumab: 141 (49.8) Reported ARD (95% CI): 0.0 (−8.2 to 8.2) Calculated RR (95% CI): 1.0 (0.85 to 1.2) N (%) PASI 100 Ixekizumab: 182 (64.3) Adalimumab: 117 (41.3) Reported ARD (95% CI): 23 (15.0 to 31.0) Calculated RR (95% CI): 1.6 (1.3 to 1.8) N (%) MDA Ixekizumab: 134 (47.3) Adalimumab: 116 (41) Reported ARD (95% CI): 6.4 (−1.8 to 14.5) Calculated RR (95% CI): 1.2 (0.96 to 1.4) Mean change (SE) from baseline in mCPDAI Ixekizumab: −4.4 (0.1) Adalimumab: −3.9 (0.1) Reported mean difference: −0.5 (−0.8 to −0.2)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			N (%) ACR20 Ixekizumab: 197 (69.6) Adalimumab: 195 (68.9) Reported ARD (95% CI): 0.7 (−6.9 to 8.3) Calculated RR (95% CI): 1.01 (0.91 to 1.1) N (%) ACR70 Ixekizumab: 100 (35.3) Adalimumab: 97 (34.3) Reported ARD (95% CI): 1.1 (−6.8 to 8.9) Calculated RR (95% CI): 1.03 (0.82 to 1.3) N (%) SPARCC Enthesitis Index = 0 (among those with score > 0 at baseline) Ixekizumab: 107/189 (56.6) Adalimumab: 83/171 (48.5) Reported ARD (95% CI): 8.1 (−2.2 to 18.4) Calculated RR (95% CI): 1.2 (0.96 to 1.4) N (%) LEI Enthesitis Index = 0 (among those with score > 0 at baseline) Ixekizumab: 98/159 (61.6) Adalimumab: 84/147 (57.1) Reported ARD (95% CI): 4.5 (−6.5 to 15.5) Calculated RR (95% CI): 1.1 (0.90 to 1.3) N (%) LDI-B Leeds Dactylitis Index = 0 (among those with score >0 at baseline) Ixekizumab: 35/42 (83.3) Adalimumab: 47/58 (81) Reported ARD (95% CI): 2.3 (−12.8 to 17.4) Calculated RR (95% CI): 1.03 (0.86 to 1.2) N (%) PASI 75 Ixekizumab: 222 (78.4) Adalimumab: 194 (68.6) Reported ARD (95% CI): 9.9 (2.7 to 17.1) Calculated RR (95% CI): 1.1 (1.04 to 1.3) N (%) PASI 90 Ixekizumab: 206 (72.8)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Adalimumab: 153 (54.1) Reported ARD (95% CI): 18.7 (10.9 to 26.5) Calculated RR (95% CI): 1.3 (1.2 to 1.5) N (%) NAPSI fingernails = 0 (among those with score > 0 at baseline) Ixekizumab: 129/191 (67.5) Adalimumab: 104/177 (58.8) Reported ARD (95% CI): 8.8 (−1.1 to 18.6) Calculated RR (95% CI): 1.1 (0.98 to 1.3) Mean change (SE) from baseline in NAPSI Ixekizumab: 169 (0.7) Adalimumab: 154 (0.7) Reported mean difference: −2.7 (−4.6 to −0.8) N (%) ≥ 0.35-point improvement from baseline in HAQ-DI (among those with score > 0 at baseline) Ixekizumab: 168/252 (66.7) Adalimumab: 164/254 (64.6) Reported ARD (95% CI): 2.1 (−6.2 to 10.4) Calculated RR (95% CI): 1.03 (0.91 to 1.2) N (%) DLQI 0 or 1 Ixekizumab: 167 (59) Adalimumab: 138 (48.8) Reported ARD (95% CI): 10.2 (2.1 to 18.4) Calculated RR (95% CI): 1.2 (1.04 to 1.4) SF-36 PCS mean (SE) change from baseline Ixekizumab: 10.1 (0.5) Adalimumab: 9.6 (0.5) Reported mean difference (SE): 0.5 (0.7), *P* = 0.44 Subgroup analyses by concomitant methotrexate use: ixekizumab more effective in achieving ACR50 response than adalimumab in those not using methotrexate (39.7% vs. 20.2%, *P* = .002) and in those using concomitant methotrexate (38.9% vs. 30.2%, *P* = .11)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Mease et al., 2017[60] Strand et al., 2019[61] OPAL Broaden Moderate	Tofacitinib 5 mg taken orally twice daily; Tofacitinib 10 mg taken orally twice daily; Adalimumab 40 mg subcutaneously every 2 weeks; or Placebo (with a switch to the 5-mg dosage of tofacitinib at month 3, or placebo with a switch to the 10-mg dosage of tofacitinib at month 3)	Tofacitinib 5 mg bid: 107 Tofacitinib 10 mg bid: 104; Adalimumab: 106 Placebo: 105 Total: 422	*Primary outcome at 3 months* Results by adalimumab vs. tofacitinib 10 mg vs. tofacitinib 5 mg; no statistical testing between active arms **ACR20** 52% vs. 61% vs. 50% **HAQ-DI** −0.38 vs. −0.40 vs. −0.35 *At 12 months* **ACR20** 60% vs. 70% vs. 68% **HAQ-DI** −0.45 vs. −0.51 vs. −0.54 *Secondary outcomes* *At 3 months* **PASI 75** 39% vs. 44% vs. 43% **ACR50** 33% vs. 40%. vs. 28% **ACR70** 19% vs. 14%. vs. 17% *At 12 months* **PASI 75** 56% vs. 67% vs. 56% **ACR50** 41% vs. 48%. vs. 45% **ACR70** 29% vs. 31%. vs. 23% **Modified Total Sharp Score** 98% vs. 95% vs. 96% *Post hoc analyses of PROs* *At 3 months, mean (SE) change* Tofacitinib 5 mg **PtGA-VAS** −20.08 (2.28) **Pain VAS** −21.49 (2.33) **SF-36 PCS:** 5.51 (0.73) **SF-36 MCS:** 4.35 (0.91) **FACIT-F** 7.0 (0.85) **EQ-VAS** 14.00 (2.10) Tofacitinib 10 mg **PtGA-VAS** −25.50 (2.29) **Pain VAS** −27.10 (2.34) **SF-36 PCS** 5.69 (0.74) **SF-36 MCS** 4.20 (0.91) **FACIT-F** 6.0 (0.85) **EQ-VAS** 15.83 (2.09) Adalimumab 40 mg	**% (N) AE** (reported through month 3) Tofacitinib 10 mg: 45% (47/104) Tofacitinib 5 mg: 39% (42/107) Adalimumab 46% (49/106) **% (N) withdrawals due to AE** Tofacitinib 10 mg: 0 Tofacitinib 5 mg: 3% (3/107) Adalimumab: 2% (2/106) **% (N) SAE** Tofacitinib 10 mg: 1% (1/104) Tofacitinib 5 mg: 3% (3/107) Adalimumab: 1% (1/106)	Minimal cases of AEs of special interest Tofacitinib 10 mg: 1 case of nonmelanoma ski cancer, Tofacitinib 5 mg: 4 incidents: 1 herpes zoster infection, 1 opportunistic infection, and 2 cases of cancer (excluding nonmelanoma skin cancer)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			PtGA-VAS −21.47 (2.33) **Pain VAS** −21.87 (2.39) **SF-36 PCS:** 6.23 (0.75) **SF-36 MCS:** 3.13 (0.94) **FACIT-F**: 6.0 (0.87) **EQ-VAS:** 13.10 (2.14)		
Mease et al., 2017[66] SPIRIT-P1 Moderate	Ixekizumab 80 mg once every 2 weeks[b]; Ixekizumab 80 mg once every 4 weeks; adalimumab 40 mg once every 2 weeks; placebo Stable doses of DMARDs, oral corticosteroids, opiates and/or NSAIDs/COX2 inhibitors allowed. At 16 weeks inadequate responders got concomitant medications, but if on adalimumab were reassigned to ixekizumab at week 24.	Ixekizumab 80 mg every 2 weeks: 103 Ixekizumab 80 mg every 4 weeks: 107 Adalimumab: 101 Placebo: 106 Total: 417	*Primary outcome at 24 weeks* Results presented by adalimumab, ixekizumab 2-wk, ixekizumab 4-wk. No statistical testing between the active arms. **ACR20** 57% vs. 62% vs. 58% *Secondary outcomes at 24 weeks* **ACR50** 39% vs. 47% vs. 40% **ACR70** 26% vs. 34% vs. 23% **% BSA** −10% vs. −11% vs. −12% **DAS-CRP** −1.74 vs. −2.04 vs. −1.96 **PASI 75** 54% vs. 80% vs. 71% **PASI 90** 37% vs. 68% vs. 56% **PASI 100** 24% vs. 53% vs. 43% **HAQ-DI** −0.37 vs. −0.50 vs. −0.44	*At 24 weeks* **% (N) treatment-emergent AE** Adalimumab: 64% (65/101) Ixekizumab 2-wk: 66% (67/102) Calculated RR, 1.02 (0.83 to 1.3) Ixekizumab 4-wk: 66% (71/107) **% (N) SAE** Adalimumab: 5% (5/101) Ixekizumab 2-wk: 3% (3/102) Calculated RR, 0.59; 95% CI, 0.15 to 2.4 Ixekizumab 4-wk: 6% (6/107) **% (N) withdrawal due to AE** Adalimumab: 2% (2/101) Ixekizumab 2-wk: 4% (4/102) Calculated RR, 2.0; 95% CI, 0.37 to 10.6 Ixekizumab 4-wk: 2%	**Injection-site reactions** Adalimumab: 2% (2/101) Ixekizumab 2-wk: 16% (16/102) Ixekizumab 4-wk: 12% (13/107) Calculated RR, 7.9; 95% CI, 1.9 to 33.6 Infection: Adalimumab: 26% (26/101) Ixekizumab 2-wk: 24% (24/102) Ixekizumab 4-wk: 28% (30/107)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
				(2/107)	
Papp et al., 2018[54] NCT02931838 Moderate	Placebo 5 oral doses of Deucravacitinib (3 mg every other day, 3 mg daily, 3 mg twice daily, 6 mg twice daily, or 12 mg daily).	Placebo: 45 Deucravacitinib 3 mg every other day: 44 Deucravacitinib 3 mg daily: 44 Deucravacitinib 3 mg twice daily: 45 Deucravacitinib 6 mg twice daily: 45 Deucravacitinib 12 mg daily: 44 Total: 268 randomized/267 analyzed	*Primary outcome at week 12* **N (%) PASI 75**; *P* value vs. placebo Placebo: 3 (7) Deucravacitinib 3 mg every other day: 4 (9); *P* = .49 Deucravacitinib 3 mg daily: 17 (39); *P* < .001 Deucravacitinib 3 mg twice daily: 31 (69); *P* < .001 Deucravacitinib 6 mg twice daily: 30 (67); *P* < .001 Deucravacitinib 12 mg daily: 33 (75); *P* < .001 *Secondary outcomes at week 12* **N (%) PASI 90**; difference vs. Placebo (95% CI) Placebo: 1 (2) Deucravacitinib 3 mg every other day: 3 (7); 5% (–16% to 25%) Deucravacitinib 3 mg daily: 7 (16). 14& (–7% to 33%) Deucravacitinib 3 mg twice daily: 20 (44); 42% (21% to 60%) Deucravacitinib 6 mg twice daily: 20 (44); 42% (21% to 60%) Deucravacitinib 12 mg daily: 19 (43); 41% (20% to 58%) **N (%) PASI 100**; difference vs. placebo (95% CI) Placebo: 0 (0) Deucravacitinib 3 mg every other day: 1 (2) 2% (–18% to 23%) Deucravacitinib 3 mg daily: 0 (0); 0% Deucravacitinib 3 mg twice daily: 4 (9); 9% (–13% to 30%) Deucravacitinib 6 mg twice daily: 8 (18); 18% (–4% to 38%)	**N (%) AE**, Calculated RR (95% CI) vs. placebo Placebo: 23 (51) Deucravacitinib 3 mg every other day: 26 (59) 1.16 (0.79 to 1.69) Deucravacitinib 3 mg daily: 24 (55) 1.07 (0.72 to 1.58) Deucravacitinib 3 mg twice daily: 29 (64) 1.26 (0.88 to 1.81) Deucravacitinib 6 mg twice daily: 36 (80) 1.57 (1.14 to 2.16) Deucravacitinib 12 mg daily: 34 (77) 1.51 (1.09 to 2.10) **N (%) SAE** Calculated RR (95% CI) vs. placebo Placebo: 1 (2) Deucravacitinib 3 mg every other day: 1 (2) 1.02 (0.70 to 15.84) Deucravacitinib 3 mg daily: 1 (2) 1.02 (0.70 to 15.84) Deucravacitinib 3 mg twice daily: 1 (2) 1 (0.065 to 15.5)	**N (%) deaths**: 0 (0) Most frequent AEs: Nasopharyngitis, headache, diarrhea, nausea, upper respiratory infection SAE included 2 events in 1 patient in the placebo group (hemorrhagic anemia and hemorrhoidal hemorrhage), 1 event in 1 patient in the 3 mg every other day group (gastroenteritis due to rotavirus), 1 patient in the 3 mg daily group (accidental eye injury), and 1 patient in the 3 mg twice daily group (dizziness due to vestibular

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Deucravacitinib 12 mg daily: 11 (25); 25% (4% to 44%) **N (%) PGA 0 or 1**; difference vs. placebo (95% CI) Placebo: 3 (7) Deucravacitinib 3 mg every other day: 9 (20); 14% (−7% to 33%) Deucravacitinib 3 mg daily: 17 (39); 32% (11% to 50%) Deucravacitinib 3 mg twice daily: 34 (76); 69% (51% to 83%) Deucravacitinib 6 mg twice daily: 29 (64); 58% (38% to 74%) Deucravacitinib 12 mg daily: 33 (75); 68% (50% to 82%) **N (%) DLQI 0 or 1;** difference vs. placebo (95% CI) Placebo: 2 (4) Deucravacitinib 3 mg every other day: 7 (16); 12% (−2% to 26%) Deucravacitinib 3 mg daily: 7 (16); 12% (-2% to 26%) Deucravacitinib 3 mg twice daily: 19 (42); 38% (20% to 54%) Deucravacitinib 6 mg twice daily: 27 (60); 56% (38% to 71%) Deucravacitinib 12 mg daily: 28 (64); 59% (41% to 74%)	Deucravacitinib 6 mg twice daily: 0 (0) 1.0 (0.004 to 252) Deucravacitinib 12 mg daily: 0 (0) 1.0 (0.004 to 257) **N (%) AE leading to withdrawal**; Calculated RR(95% CI) vs. placebo Placebo: 2 (4) Deucravacitinib 3 mg every other day: 1 (2) 0.51 (0.05 to 5.44) Deucravacitinib 3 mg daily: 2 (5) 1.02 (0.15 to 6.9) Deucravacitinib 3 mg twice daily: 1 (2) 0.50 (0.05 to 5.3) Deucravacitinib 6 mg twice daily: 3 (7) 1.57 (1.1 to 2.2) Deucravacitinib 12 mg daily: 1 (2) 0.51 (0.05 to 5.4)	dysfunction). In addition, 1 case of in situ melanoma was diagnosed on skin biopsy of an atypical nevus at day 96 after the first doses of 3 mg daily.
Papp et al., 2018[38] BE ABLE-1 Moderate	Bimekizumab administered SC every 4 weeks at doses of 64 mg, 160 mg, 160 mg (with 320 mg loading dose at baseline), 320 mg,	Placebo: 42, Bimekizumab 64 mg: 39 Bimekizumab 160 mg:43 Bimekizumab 160 mg (320 mg at baseline):	*Primary outcome at week 12* **% PASI 90** All bimekizumab doses: 46.2% to 79.1% Placebo: 0%; *P* < .001, all comparisons *Secondary outcomes* **% PASI 90 at week 8** All bimekizumab doses: 41.0% to 86.0% Placebo: 0%; *P* < .001, all comparisons	**N (%) TEAE** All bimekizumab doses: 126 (61) Placebo: 15 (36) Calculated RR, 1.7; 95% CI, 1.1 to 2.6 **N (%) SAE** All bimekizumab	Deaths: 0 (0) Most common AEs were nasopharyngitis, upper respiratory infection, arthritis,

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	480 mg, or placebo. Treatment was administered at baseline, week 4, and week 8 for a total of 3 injections.	40 Bimekizumab 320 mg:43 Bimekizumab 480 mg: 43 Total: 250	**% PASI 75 at week 12** All bimekizumab doses: 61.5% to 93.0% Placebo: 4.8%; *P* < .001, all comparisons **% PASI 100 at week 12** All bimekizumab doses: 27.9% to 60.0% Placebo: 0%; *P* ≤ .001, all comparisons **% IGA 0 or 1 at week 8** All bimekizumab doses: 46.2% to 86.0% Placebo: 4.8%; *P* < .001, all comparisons **% IGA 0 or 1 at week 12** All bimekizumab doses: 51.3% to 86.0% Placebo: 4.8%; *P* ≤ .001, all comparisons	doses: 1 (0.5) polyp and colon cancer Placebo: 1 (2.3) viral meningitis Calculated RR, 0.20; 95% CI, 0.01 to 3.2 None of the SAEs were considered related to the study treatment by study investigators **N (%) severe AE** [severe was undefined] All bimekizumab doses: 2 (4.7) Placebo: 0(0) **N (%) withdrawals due to AE** All bimekizumab doses: 10 (4.8) Placebo: 1 (2.4) Calculated RR, 2.0; 95% CI, 0.27 to 15.4	elevated liver enzyme, hypertension
Papp et al., 2017[52] None Moderate	Risankizumab 18 mg SC once on day 0 Risankizumab 90 mg SC at weeks 0, 4, and 16 Risankizumab 180 mg SC at weeks 0, 4, and 16 Ustekinumab 45	Risankizumab once: 43 Risankizumab 90 mg: 41 Risankizumab 180 mg: 42 Ustekinumab: 40 Total: 166	*Primary outcome at week 12* *Study authors pooled the 90-mg and 190-mg risankizumab dosages.* **% PASI 90** 77% (risankizumab) vs. 40% (ustekinumab), *P* < .001 *Secondary outcomes at week 12* **% PASI 50** 96% (risankizumab) vs. 82% (ustekinumab), *P* < .001 **% PASI 75** 93% (risankizumab) vs. 88% (ustekinumab), *P* < .001 **% PASI 100** 45% (risankizumab) vs. 18%	*Safety data are through week 48* **% AE** 81% risankizumab 18 mg 80% risankizumab 90 mg 69% risankizumab 180 mg 72% ustekinumab, *P* = NR Treatments did not differ with regard to	Most common AE (occurring in > 10% of the participants) in all treatment groups: nasopharyngitis. No deaths reported

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	or 90 mg (if patient weight more than 100 kg) at weeks 0, 4, and 16 48 weeks		(ustekinumab), *P* < .001 **% PGA 0 or 1** 89% (risankizumab) vs. 62% (ustekinumab), *P* < .001 **% DLQI 0 or 1** 72% (risankizumab) vs. 53% (ustekinumab), *P* < .001	overall incidences of adverse events (*P* = 0. 299) **% SAE** 5 (12%) risankizumab 18 mg 6 (15%) risankizumab 90 mg 0 risankizumab 180 mg 3 (8%) ustekinumab **% withdrawals due to AE** 1 risankizumab 18 mg, 1 risankizumab 90 mg 0 risankizumab 180 mg 1 ustekinumab	
Reich et al., 2021[24] BE RADIANT Moderate	Bimekizumab 320 mg SC every 4 weeks to week 16 then every 4 weeks or every 8 weeks to week 48 Secukinumab 300 mg SC weekly to week 4 then every 4 weeks to week 48	Bimekizumab: 373 (those who completed week 16 were rerandomized to continue every 4 weeks (147) or change to every 8 weeks (215)) Secukinumab: 370 Total: 743	At 16 weeks Primary outcome N (%) PASI 100 Bimekizumab: 230 (61.7) Secukinumab: 181 (48.9) Reported ARD (95% CI): 12.7 (5.8 to 19.6) Calculated RR (95% CI): 1.3 (1.1 to 1.4) Secondary outcomes N (%) PASI 90 Bimekizumab: 319 (85.5) Secukinumab: 275 (74.3) Calculated RR (95% CI): 1.2 (1.1 to 1.2) N (%) PASI 75 Bimekizumab: 348 (93.3) Secukinumab: 337 (91.1) Calculated RR (95% CI): 1.02 (0.98 to 1.1) N (%) IGA 0 or 1 Bimekizumab: 319 (85.5) Secukinumab: 291 (78.6)	N (%) any AE Bimekizumab: 321 (86.1) Secukinumab: 301 (81.4) Calculated RR (95% CI): 1.06 (0.99 to 1.1) N (%) serious AE Bimekizumab: 22 (5.9) Secukinumab: 21 (5.7) Calculated RR (95% CI): 1.04 (0.58 to 1.9) N (%) discontinuations due to AE Bimekizumab: 13 (3.5) Secukinumab: 10 (2.7) Calculated RR (95% CI): 1.3 (0.57 to 2.9) N (%) drug-related AE	N (%) serious infections Bimekizumab: 8 (2.1) Secukinumab: 8 (2.2) N (%) mortality Bimekizumab: 1 (0.3) Secukinumab: 1 (0.3) N (%) cancer Bimekizumab: 5 (1.3) Secukinumab: 3 (0.8) N (%) adjudicated MACE

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Calculated RR (95% CI): 1.1 (1.02 to 1.2) At 48 weeks N (%) PASI 100 Bimekizumab: 250 (67.0) Secukinumab: 171 (46.2) Reported ARD (95% CI): 20.9 (14.1 to 27.7) Calculated RR (95% CI): 1.5 (1.3 to 1.7) N (%) PASI 90 Bimekizumab: 312 (83.6) Secukinumab: 261 (70.5) Calculated ARD (95% CI): 13.1 (7.1 to 19.1) Calculated RR (95% CI): 1.2 (1.1 to 1.3) N (%) PASI 75 Bimekizumab: 330 (88.5) Secukinumab: 301 (81.4) Reported ARD (95% CI): 7.1 (2.0 to 12.2) Calculated RR (95% CI): 1.09 (1.02 to 1.2) N (%) IGA 0 or 1 Bimekizumab: 313 (83.9) Secukinumab: 273 (73.8) Calculated ARD (95% CI): 10.1 (4.3 to 16.0) Calculated RR (95% CI): 1.1 (1.06 to 1.2) N (%) DLQI 0 or 1 Bimekizumab: 290 (77.7) Secukinumab: 260 (70.3) Calculated ARD (95% CI): 7.5 (1.2 to 13.8) Calculated RR (95% CI): 1.1 (1.02 to 1.2) N (%) PASI 100 Bimekizumab every 4 weeks: 108 (73.5) Bimekizumab every 8 weeks: 142 (66.0) Secukinumab: 171 (48.3) Bimekizumab every 4 weeks vs. secukinumab Reported ARD (95% CI): 26.5 (17.9 to 35.1), *P* < .001 Calculated RR (95% CI): 1.5 (1.3 to 1.8)	Bimekizumab: 160 (42.9) Secukinumab: 117 (31.6)	Bimekizumab: 0 (0) Secukinumab: 2 (0.5)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Bimekizumab every 8 weeks vs. secukinumab: Reported ARD (95% CI): 17.3 (9.3 to 25.3), *P* < .001 Calculated RR (95% CI): 1.4 (1.2 to 1.6) N (%) PASI 90 Bimekizumab every 4 weeks: 126 (85.7) Bimekizumab every 8 weeks: 186 (86.5) Secukinumab: 261 (73.7) Bimekizumab every 4 weeks vs. secukinumab Reported ARD (95% CI): 12.8 (5.7 to 19.9) Calculated RR (95% CI): 1.2 (1.06 to 1.3) Bimekizumab every 8 weeks vs. secukinumab: Reported ARD (95% CI): 12.3 (5.9 to 18.6) Calculated RR (95% CI): 1.2 (1.08 to 1.3) N (%) PASI 75 Bimekizumab every 4 weeks: 134 (91.2) Bimekizumab every 8 weeks: 196 (91.2) Secukinumab: 301 (85.0) Bimekizumab every 4 weeks vs. secukinumab Reported ARD (95% CI): 6.6 (0.7 to 12.5) Calculated RR (95% CI): 1.07 (1.003 to 1.1) Bimekizumab every 8 weeks vs. secukinumab Reported ARD (95% CI): 5.8 (0.6 to 11.0) Calculated RR (95% CI): 1.07 (1.009 to 1.1) N (%) IGA 0 or 1 Bimekizumab every 4 weeks: 128 (87.1) Bimekizumab every 8 weeks: 185 (86.0) Secukinumab: 273 (77.1) Bimekizumab every 4 weeks vs. secukinumab Reported ARD (95% CI): 11.0 (4.1 to 17.9) Calculated RR (95% CI): 1.1 (1.04 to 1.2) Bimekizumab every 8 weeks vs. secukinumab: Reported ARD (95% CI): 8.3 (2.1 to 14.5) Calculated RR (95% CI): 1.1 (1.03 to 1.2)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Reich et al., 2021[21] BE VIVID Moderate	Bimekizumab 320 mg SC every 4 weeks for 52 weeks Ustekinumab 45 mg (≤100 kg) or 90 mg SC (>100 kg) at weeks 0 and 4 then every 12 weeks for 52 weeks Placebo every 4 weeks for 16 weeks. At week 16, participants in placebo group received bimekizumab 320 mg every 4 weeks up to 52 weeks	Placebo: 83 Bimekizumab: 321 Ustekinumab: 163 Total: 567	At week 16 Primary outcomes N (%) PASI 90 Bimekizumab: 273 (85) Placebo: 4 (5) Ustekinumab: 81 (50) Bimekizumab vs. placebo Reported OR (95 CI): 99.9 (34.0 to 293.2), *P* < .0001 Reported ARD (95% CI): 80 (74 to 86) Calculated RR (95% CI): 17.7 (6.8 to 46.0), *P* < .001 Bimekizumab vs. ustekinumab Reported OR (95 CI): 6.1 (3.9 to 9.5), *P* < .0001 Reported ARD (95% CI): 35 (27 to 43) Calculated RR (95% CI): 1.7 (1.5 tp 2.0), *P* < .001 N (%) IGA 0 or 1 Bimekizumab: 270 (84) Placebo: 4 (5) Ustekinumab: 87 (53) Bimekizumab vs. placebo Reported OR (95 CI): 118.8 (36.7 to 384.3), *P* < .0001 Reported ARD (95% CI): 79 (73 to 85) Calculated RR (95% CI): 17.5 (6.7 to 45.5), *P* < .001 Bimekizumab vs. ustekinumab Reported OR (95 CI): 4.8 (3.1 to 7.5), *P* < .0001 Reported ARD (95% CI): 30 (22 to 39) Calculated RR (95% CI): 1.6 (1.4 to 1.8), *P* < .001 Secondary outcomes N (%) PASI 100 Bimekizumab: 188 (59) Placebo: 0 (0) Ustekinumab: 34 (21)	At 16 weeks N (%) any TEAE Bimekizumab: 181 (56) Placebo: 39 (47) Ustekinumab: 83 (51) Calculated RR (95% CI) Bimekizumab vs. placebo: 1.2 (0.94 to 1.5) Bimekizumab vs. ustekinumab: 1.1 (0.93 to 1.3) N (%) serious TEAE Bimekizumab: 5 (2) Placebo: 2 (2) Ustekinumab: 5 (3) Calculated RR (95% CI) Bimekizumab vs. placebo: 0.65 (0.13 to 3.3) Bimekizumab vs. ustekinumab: 0.51 (0.15 to 1.7) N (%) discontinuations due to TEAE Bimekizumab: 6 (2) Placebo: 6 (7) Ustekinumab: 3 (2) Calculated RR (95% CI) Bimekizumab vs. placebo: 0.26 (0.09 to 0.78) Bimekizumab vs. ustekinumab: 1.0 (0.26 to 4.0)	N (%) serious infections Bimekizumab: 0 (0) Placebo: 0 (0) Ustekinumab: 2 (1) N (%) mortality Bimekizumab: 1 (0.31) Placebo: 1 (1) Ustekinumab: 1 (1) N (%) malignancies Bimekizumab: 0 (0) Placebo: 1 (1) Ustekinumab: 0 (0) N (%) adjudicated major adverse cardiovascular events Bimekizumab: 1 (0.31) Placebo: 0 (0) Ustekinumab: 0 (0)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Bimekizumab vs. placebo Reported OR (95 CI): 25.6 (9.1 to 72.3), *P* < .0001 Reported ARD (95% CI): 59 (53 to 64) Calculated RR NA (0 events in 1 group) Bimekizumab vs. ustekinumab Reported OR (95 CI): 5.7 (3.6 to 8.9), *P* < .0001 Reported ARD (95% CI): 38 (30 to 46) Calculated RR (95% CI): 2.8 (2.1 to 3.8), *P* < .001 N (%) IGA 0 Bimekizumab: 188 (59) Placebo: 0 (0) Ustekinumab: 36 (22) Bimekizumab vs. placebo Reported OR (95 CI): 25.5 (9.0 to 71.9), *P* < .0001 Reported ARD (95% CI): 59 (53 to 64) Calculated RR NA (0 events in 1 group) Bimekizumab vs. ustekinumab Reported OR (95 CI): 5.2 (3.4 to 8.1), *P* < .0001 Reported ARD (95% CI): 37 (29 to 45) Calculated RR (95% CI): 2.7 (2.0 to 3.6), *P* < .001 N (%) DLQI 0 or 1 Bimekizumab: 216 (67) Placebo: 10 (12) Ustekinumab: 69 (42) Bimekizumab vs. placebo Reported nominal *P* < .0001 Calculated RR (95% CI): 5.6 (3.1 to 10.0), *P* < .001 Bimekizumab vs. ustekinumab Reported nominal *P* < .0001 Calculated RR (95% CI): 1.6 (1.3 to 1.9), *P* < .001 Other secondary outcomes reported (P-SIM itch and scaling scores; scalp IGA response) showed significantly larger improvements for bimekizumab vs. placebo and vs. ustekinumab; P-SIM pain was not significantly different when vs.		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			ustekinumab. Secondary outcomes at week 52 (includes placebo group switched to Bimekizumab at week 16) N (%) PASI 90 Bimekizumab: 263 (82) Ustekinumab: 91 (56) Reported OR (95 CI): 3.8 (2.4 to 5.9), *P* < .0001 Reported ARD (95% CI): 26 (17 to 34) Calculated RR (95% CI): 1.5 (1.3 to 1.7), *P* < .001 N (%) IGA 0 or 1 (includes placebo group switched to bimekizumab at week 16) Bimekizumab: 251 (78) Ustekinumab: 99 (61) Reported OR (95 CI): 2.4 (1.6 to 3.7), *P* < .0001 Reported ARD (95% CI): 17 (9 to 26) Calculated RR (95% CI): 1.3 (1.1 to 1.5), *P* < .001 N (%) PASI 75 (does not include placebo group switched to bimekizumab at week 16) Bimekizumab: 273 (85) Ustekinumab: 121 (74) Calculated RR (95% CI): 1.1 (1.04 to 1.3), *P* = .005 Calculated ARD (95% CI): 10.8 (3.0 to 18.6) N (%) PASI 100 (does not include placebo group switched to bimekizumab at week 16) Bimekizumab: 209 (65) Ustekinumab: 62 (38) Reported nominal *P* < .0001 Calculated RR (95% CI): 1.7 (1.4 to 2.1), *P* < .001 Calculated ARD (95% CI): 26.5 (17.3 to 35.6) N (%) IGA 0 (does not include placebo group switched to bimekizumab at week 16) Bimekizumab: 209 (65) Ustekinumab: 66 (39) Calculated RR (95% CI): 1.6 (1.3 to 2.0), *P* < .001		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Calculated ARD (95 CI%): 24.6 (15.4 to 33.8) N (%) DLQI 0 or 1 (does not include placebo group switched to bimekizumab at week 16) Bimekizumab: 241 (75) Ustekinumab: 103 (63) Calculated RR (95% CI): 1.2 (1.04 to 1.4), *P* = .007 Calculated ARD (95% CI): 11.9 (3.1 to 20.7)		
Reich et al., 2017[73] Reich et al., 2019[71] Gordon et al., 2018[72] Puig et al., 2021[84] VOYAGE-2 Moderate	Adalimumab SC 80 mg at week 0, 40 mg at week 1 and every 2 weeks Guselkumab SC 100 mg at weeks 0, 4, 12 This study also included a placebo arm.	Placebo: 248 Adalimumab 40 mg: 248, Guselkumab 100 mg: 496 Total: 992	*Primary outcomes at week 16* **N (%) IGA 0 or 1** Guselkumab: 417 (84.1) Adalimumab: 168 (67.7) ARD*, 16.3%; 95% CI, 9.7% to 23.0% Calculated RR, 1.2; 95% CI, 1.1 to 1.4 **N (%) PASI 90** Guselkumab: 347 (70.0) Adalimumab: 116 (46.8) ARD* 23.2%; 95% CI, 15.8% to 30.6% Calculated RR, 1.5; 95% CI, 1.3 to 1.7 *Secondary outcomes at week 16* **N (%) IGA 0** Guselkumab: 215 (43.3) Adalimumab: 71 (28.6) ARD* 14.7%; 95% CI, 7.6% to 21.8% Calculated RR, 1.5; 95% CI, 1.2 to 1.9 **N (%) PASI 100** Guselkumab: 169 (34.1) Adalimumab: 51 (20.6) ARD*, 13.5%; 95% CI, 7.0% to 20.1% Calculated RR, 1.7; 95% CI, 1.3 to 2.2 **N (%) PASI 75** Guselkumab: 428 (86.3) Adalimumab: 170 (68.5) ARD*, 17.7%; 95% CI, 11.2% to 24.3% Calculated RR, 1.3; 95% CI, 1.1 to 1.4 **Mean (SD) change in SF-36 PCS**	**N (%) AE** Guselkumab: 235 (47.6) Adalimumab: 120 (48.4) Calculated RR, 0.98 (95% CI, 0.84 to 1.2) **N (%) SAE** Guselkumab: 8 (1.6) Adalimumab: 6 (2.4) Calculated RR, 0.67 (95% CI, 0.25 to 1.9) **N (%) withdrawal due to AEs** Guselkumab: 7 (1.4) Adalimumab: 4 (1.6) Calculated RR, 0.88 (95% CI, 0.26 to 3.0) **VOYAGE-1 and VOYAGE-2** Subgroup analysis at week 16 Compared with guselkumab, AE frequency was numerically greater in adalimumab treated	**N (%) infections** Guselkumab: 106 (21.5) Adalimumab: 58 (23.4) Calculated RR, 0.92 (95% CI, 0.69 to 1.2) **N (%) with injection-site reactions** Guselkumab: 13*(2.6) Adalimumab: 21* (6.9) Calculated RR, 0.38 (0.19 to 0.74) The most common AEs include nasopharyngitis, headache, and upper respiratory tract infection.

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Guselkumab: 5.46 (7.8) Adalimumab: 3.92 (6.6) AMD*, 1.54; 95% CI, 0.40 to 2.7; *P* = .008 **Mean (SD) change in SF-36 MCS** Guselkumab: 5.66 (9.5) Adalimumab: 4.57 (9.4) AMD* 1.09; 95% CI, −0.36 to 2.54; *P* = .14 **Mean (SD) change in DLQI** Guselkumab: −11.3 (6.8) Adalimumab: −9.7 (6.8) AMD*, −1.6; 95% CI, −2.6 to −0.6; *P* = .003 **N (%) DLQI 0 or 1** Guselkumab: 254 (51.7) Adalimumab: 96 (39.0) ARD*, 13.0%; 95% CI, 5.5% to 20.5% Calculated RR, 1.3; 95% CI, 1.1 to 1.6 **Mean (SD) change in PSSD symptom score** Guselkumab: −40.4 (26.5) Adalimumab: −32.8 (24.9) AMD, −7.6; 95% CI, −12.0 to −3.2; *P* < .001 **Mean (SD) change in PSSD sign score** Guselkumab: −42.9 (23.7) Adalimumab: −34.6 (23.5) AMD*, −8.3; 95% CI, −12.3 to −4.3; *P* < .001 **Mean (SD) change in HADS-A** Guselkumab: −1.7 (3.4) Adalimumab: −1.1 (3.4) AMD*, −0.6; 95% CI, −1.1 to −0.08; *P* = .02 **Mean (SD) change in HADS-D** Guselkumab: −1.6 (3.6) Adalimumab: −1.2 (3.4) AMD*, −0.4; 95% CI, −0.94 to 0.14; *P* = .14 **VOYAGE-1 and VOYAGE-2** Subgroup analysis at week 16 No significant differences in treatment effect	participants in the Hispanic population but not the non-Hispanic population (no specific pattern accounted for the difference); SAEs, major adverse cardiovascular events, malignancies other than nonmelanoma skin cancer, and nonmelanoma skin cancer occurred infrequently across all treatment groups in both the Hispanic and non- Hispanic populations.	

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			comparing guselkumab vs. adalimumab as measured by DLQI 0 or 1, IGA 0 or 1, PASI 90, PASI 75, PASI 100, between those who are Hispanic and those who are non-Hispanic.		
Reich et al., 2019[44] Blauvelt et al., 2021[80] ECLIPSE Moderate	Guselkumab 100 mg SC at 0, 4, 12 weeks and then every 8 weeks until week 44. Secukinumab 300 mg as 2 150-mg SC injections at 0, 1, 2, 3, and 4, and then every 4 weeks until week 44. The guselkumab group received placebo injection to match the number of injections in the secukinumab group.	Guselkumab: 534 Secukinumab: 514 Total: 1,048	*Primary outcome at week 48* **N (%) PASI 90** Guselkumab: 451 (84) Secukinumab: 360 (70) Noninferiority *P* < .001 Superiority *P* < .001 *Secondary outcomes* **N (%) PASI 75 at both week 12 and week 48** Guselkumab: 452 (85) Secukinumab: 412 (80) Noninferiority *P* < .001 Superiority *P* = .062 **N (%) PASI 90 at week 12** Guselkumab: 369 (69) Secukinumab: 391 (76) No significance testing done to control for type I error. **N (%) PASI 75 at week 12** Guselkumab: 477 (89) Secukinumab: 471 (92) No significance testing done to control for type I error. **N (%) PASI 100 at week 48** Guselkumab: 311 (58) Secukinumab: 249 (48) No significance testing done to control for type I error. **N (%) IGA 0 at week 48** Guselkumab: 332 (62) Secukinumab: 259 (50) No significance testing done to control for type I	**N (%) AE** Guselkumab: 416 (78) Secukinumab: 417 (82) Calculated RR, 0.95; 95% CI, 0.90 to 1.02 **N (%) SAE** Guselkumab: 33 (6) Secukinumab: 37 (7) Calculated RR, 0.85; 95% CI, 0.54 to 1.3 **N (%) withdrawal because of AE** Guselkumab: 10 (2) Secukinumab: 12 (2) Calculated RR, 0.80; 95% CI, 0.35 to 1.8	**N (%) infections** Guselkumab: 313 (59) Secukinumab: 331 (65) The most common AEs were nasopharyngitis, upper respiratory tract infection, headache, arthralgia, back pain, diarrhea.

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			error. **N (%) IGA 0 or 1 at week 48** Guselkumab: 454 (85) Secukinumab: 385 (75) No significance testing done to control for type I error. *Subgroup analysis at week 48* Larger proportions of participants in the guselkumab group than the secukinumab group achieved PASI 90, PASI 100, IGA 0/1, and IGA 0 for all body weight subgroups (ranging in 10-kg increments from 60 kg to > 110 kg) with the greatest differences seen in the > 100 kg groups; all BMI subgroups (< 25 kg/m^2, ≥25 kg to < 30 kg/m^2, ≥ 30 kg/m^2); all age groups (< 45 years, 45 to < 65 years, and ≥ 65 years); all baseline disease severity categories; and history of previous psoriasis medication.		
Reich et al., 2019[46] IMMVent Moderate	Risankizumab 150 mg SC at weeks 0 and 4; Adalimumab 80 mg SC at week 0 and then 40 mg every other week from week 1 up to the end of week 15.	Risankizumab 150 mg: 301 Adalimumab 40 mg: 304 Total: 605	*Primary outcomes at week 16* **N (%) PASI 90** Adalimumab: 144 (47%) Risankizumab: 218 (72%) ARD, 24.9%; 95% CI, 17.5% to 32.4%; *P* < .001 **N (%) PGA 0 or 1** Adalimumab: 183 (60%) Risankizumab: 252 (84%) ARD, 23.3%; 95% CI, 16.6% to 30.1%; *P* < .001 *Secondary outcomes at week 16* **N (%) PGA 0** Adalimumab: 71 (23%) Risankizumab: 124 (41%) ARD, 17.7%; 95% CI, 10.4% to 24.9%; *P* < .001 **N (%) PASI 100** Adalimumab: 70 (23%)	**N (%) AE** Adalimumab: 173 (57%) Risankizumab: 168 (56%) Calculated RR, 0.98 (95% CI, 0.85 to 1.1) **N (%) SAE** Adalimumab: 9 (3%) Risankizumab: 10 (3%) Calculated RR, 1.1 (95% CI, 0.46 to 2.7) **N (%) withdrawal due to AE** Adalimumab: 6 (2%) Risankizumab: 4 (1%) Calculated RR, 0.67	**N (%) infection** Adalimumab: 74 (24%) Risankizumab: 88 (29%) Calculated RR, 1.2; 95% CI, 0.92 to 1.6 The most frequently reported AEs (occurring in ≥5% of participants in either group) were viral upper

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Risankizumab: 120 (40%) ARD, 16.7%; 95% CI, 9.5% to 23.9%; *P* < .001 **N (%) PASI 75** Adalimumab: 218 (72%) Risankizumab: 273 (91%) ARD, 18.9%; 95% CI, 13.0% to 24.9%; *P* < .001 **N (%) DLQI 0 or 1** Adalimumab: 148 (49%) Risankizumab: 198 (66%) *P* < .001 **Mean change in WLQ** Adalimumab: −1.9 Risankizumab: −2.8 *P* = .0123	(95% CI, 0.19 to 2.4)	respiratory tract infection, upper respiratory tract infection, and headache. Deaths occurred in 1 patient in the risankizumab group (acute myocardial infarction on day 73) and in 2 participants in the adalimumab group (stage IV gallbladder cancer, abdominal abscess, sepsis, and gastric perforation following gallbladder surgery). None of the deaths were considered to be related to the study drug by investigators.
Reich et al., 2017[65] Lebwohl et al., 2020[75] RESURFACE-2	Placebo (through week 12 only, then re-randomized to tildrakizumab through week 28	Placebo: 156 Etanercept: 313 Tildrakizumab 100 mg: 307 Tildrakizumab	*Primary outcome at week 12* **N (%) PASI 75** Etanercept: 151 (48) Tildrakizumab 100 mg: 188 (61) Tildrakizumab 200 mg: 206 (66) ARD vs. etanercept (95% CI,	*Weeks 0 to 12* **N (%) AE** Calculated RR (95% CI) vs. etanercept Etanercept: 169 (54) Tildrakizumab 100 mg:	*Weeks 0 to 12* **N (%) deaths** Etanercept: 0 (0) Tildrakizumab 100 mg: 1 (<1) Tildrakizumab

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Moderate	Etanercept 50 mg twice weekly through week 12 then 1 dose weekly Tildrakizumab 200 mg at baseline and week 4 and then every 12 weeks Tildrakizumab 100 mg at baseline and week 4 and then every 12 weeks	200 mg: 314 Total: 1,090	*P* value) Tildrakizumab 100 mg: 13.1% (5.3% to 20.7%, .001) Tildrakizumab 200 mg: 17.4% (9.7% to 24.9%, < .001) **N (%) PGA 0 or 1** Etanercept: 149 (48) Tildrakizumab 100 mg: 168 (55) Tildrakizumab 200 mg: 186 (59) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 7.3% (-0.5% to 15.0%, .066) Tildrakizumab 200 mg: 11.7% (4.0% to 19.3%, .003) *Secondary outcomes at week 12* **N (%) PASI 100** Etanercept: 15 (5) Tildrakizumab 100 mg: 38 (12) Tildrakizumab 200 mg: 37 (12) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 7.6% (3.3% to 12.3%, .0006) Tildrakizumab 200 mg: 7.0% (2.8% to 11.6%, .0014) **N (%) PASI 90** Etanercept: 67 (21) Tildrakizumab 100 mg: 119 (39) Tildrakizumab 200 mg: 115 (37) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 17.4% (10.3% to 24.4%, < .001) Tildrakizumab 200 mg: 15.2% (8.3% to	136 (44); 0.82 (0.70 to 0.96) Tildrakizumab 200 mg: 155 (49); 0.91 (0.79 to 1.1) N (%) **N (%) SAE** Calculated RR (95% CI) vs. etanercept Etanercept: 7 (2) Tildrakizumab 100 mg: 4 (1); 0.58 (0.17 to 2.0) Tildrakizumab 200 mg: 6 (2); 0.85 (0.29 to 2.5) **N (%) withdrawal due to AE** Calculated RR (95% CI) vs. etanercept Etanercept: 6 (2) Tildrakizumab 100 mg: 3 (1); 0.51 (0.13 to 2.0) Tildrakizumab 200 mg: 3 (1); 0.50 (0.13 to 2.0) *Weeks 13 to 28* **N (%) AE** Calculated RR (95% CI) vs. etanercept Etanercept: 164 (57) Tildrakizumab 100 mg: 135 (46); 0.81 (0.69 to 0.95) Tildrakizumab 200 mg: 135 (45); 0.80 (0.68 to 0.93) **N (%) SAE** Calculated RR (95% CI) vs.	200 mg: 0 (0) **N (%) severe infections** Etanercept: 0 (0) Tildrakizumab 100 mg: 0 (0) Tildrakizumab 200 mg: 1 (<1) **N (%) injection-site erythema** CALCULATED RR (95% CI) vs. etanercept Etanercept: 27 (9) Tildrakizumab 100 mg: 2 (1), 0.08 (0.02 to 0.31) Tildrakizumab 200 mg: 2 (1), 0.07 (0.02 to 0.31) *Weeks 13 to 28* **N (%) deaths** Etanercept: 0 (0) Tildrakizumab 100 mg: 0 (0) Tildrakizumab 200 mg: 0 (0) **N (%) severe infections** Etanercept: 3 (1) Tildrakizumab 100 mg: 1 (<1)

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			22.1%, < .001) **N (%) DLQI 0 or 1** Etanercept: 108 (36) Tildrakizumab 100 mg: 119 (40) Tildrakizumab 200 mg: 145 (47) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 4.8% (-2.9% to 12.5%, .221) Tildrakizumab 200 mg: 11.9% (4.1% to 19.5%, .003) *Subgroup analysis* No significant differences in effect and safety were observed for both tildrakizumab doses based on metabolic syndrome status. *Outcomes at 28 weeks* **N (%) PASI 75** Etanercept: 155 (54) Tildrakizumab 100 mg: 216 (73) Tildrakizumab 200 mg: 217 (73) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 20.1% (12.4% to 27.6%, <.001) Tildrakizumab 200 mg: 19.2% (11.5% to 26.7%, <.001) **N (%) PGA 0 or 1** Etanercept: 131 (45) Tildrakizumab 100 mg: 190 (65) Tildrakizumab 200 mg: 207 (69) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 19.6% (11.7% to 27.3%, <.001)	etanercept Etanercept: 14 (5) Tildrakizumab 100 mg: 9 (3); 0.63 (0.28 to 1.4) Tildrakizumab 200 mg: 6 (2); 0.41 (0.16 to 1.1) **N (%) withdrawal due to AE** Calculated RR (95% CI) vs. etanercept Etanercept: 3 (1) Tildrakizumab 100 mg: 1 (<1); 0.33 (0.03 to 3.1) Tildrakizumab 200 mg: 1 (<1); 0.32 (0.03 to 3.1)	Tildrakizumab 200 mg: 2 (1) **N (%) injection-site erythema** Calculated RR (95% CI) vs. etanercept Etanercept: 3 (1) Tildrakizumab 100 mg: 3 (1), 0.98 (0.20 to 4.8) Tildrakizumab 200 mg: 1 (<1), 0.32 (0.03 to 3.1) Most common AEs included injection-site erythema, nasopharyngitis, upper respiratory tract infection.

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Tildrakizumab 200 mg: 24.1% (16.2% to 31.7%, <.001) **N (%) PASI 90** Etanercept: 85 (29) Tildrakizumab 100 mg: 161 (55) Tildrakizumab 200 mg: 169 (57) ARD vs, etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 25.5% (17.6% to 33.0%, < .001) Tildrakizumab 200 mg: 27.3% (19.5% to 34.7%, < .001) **N (%) PASI 100** Etanercept: 31 (11) Tildrakizumab 100 mg: 66 (22) Tildrakizumab 200 mg: 79 (26) ARD vs, etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 11.8% (5.9% to 17.9%, < .001) Tildrakizumab 200 mg: 15.7% (9.6% to 22.0%, .001) **N (%) DLQI 0 or1** Etanercept: 111 (39) Tildrakizumab 100 mg: 157 (54) Tildrakizumab 200 mg: 193 (65) ARD vs. etanercept (95% CI, *P* value) Tildrakizumab 100 mg: 15.0% (6.9% to 22.9%, .0003) Tildrakizumab 200 mg: 25.7% (17.7% to 33.4%, <.001)		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Reich et al., 2017[47] Paul et al., 2018[48] Puig et al., 2020[83] Wasel et al., 2020[79] IXORA-S Moderate	Ixekizumab 80 mg[a] SC every 2 weeks through week 12, every 4 weeks thereafter Ustekinumab 45 or 90 mg SC (if patient weight more than 100 kg) at weeks 0, 4, and 16 Induction period: 12 weeks Maintenance period: 52 weeks	Ixekizumab: 136 Ustekinumab: 166 Total: 302	*Primary outcome at week 12* **% PASI 90** 72.8% (ixekizumab) vs. 42.2% (ustekinumab), *P* < .001 *Secondary outcomes at week 12* **% PASI 75** 88.2% (ixekizumab) vs. 68.7% (ustekinumab), *P* < .001 **% PASI 100** 36.0% (ixekizumab) vs. 14.5% (ustekinumab), *P* < .001 **% PGA 0 or 1** 83.6% (ixekizumab) vs. 57.2% (ustekinumab), *P* < .001 **% DLQI 0 or 1** 61.0% (ixekizumab) vs. 44.6% (ustekinumab), *P* = .012 **% Itch NRS ≥ 4-point improvement** 76.4% (ixekizumab) vs. 74.3% (ustekinumab), *P* = .70 **Skin pain VAS mean (SD) change** -35.4 (32.1) (ixekizumab) vs. 29.1 (30.7) (ustekinumab), *P* = .07 **EQ-5D-5L mean (SD) change** 0.124 (0.22) (ustekinumab) vs. 0.168 (0.23) (ixekizumab), *P* > .05 **EQ-PsO Index Score mean (SD) change** 0.117 (0.16) (ustekinumab) vs. 0.151 (0.16) (ixekizumab), *P* < .05 **EQ-5D VAS mean (SD) change** 10.10 (22.7) (ustekinumab) vs. 13.56 (22.3) (ixekizumab), *P* > .05 **WPAI-PsO change** No difference between groups (data reported in	*At week 12* **% (N) TEAEs** Ixekizumab 69.6% (94/135) vs. Ustekinumab 75.3% (125/166), *P* = .299 **% (N) Nonfatal SAE** Ixekizumab 2.2% (3/135) vs. Ustekinumab 3.0% (5/166), *P* = .735 **% (N) severe TEAE** Ixekizumab 4.4% (6/135) vs. Ustekinumab 6.0% (10/166), *P* = .613 % (N) Withdrawal due to AEs Ixekizumab 1.5% (2/135) vs. ustekinumab 0.6% (1/166), *P* = .589 *At 52 weeks* **% (N) TEAEs** Ixekizumab 86.7% (117/135) vs. ustekinumab 83.7% (139/166), *P* = .519, Calculated RR, 1.04 (95% CI< 0.94 to 1.1) **% (N) SAE** Ixekizumab 6.7% (9/135) vs. ustekinumab 3.6% (6/166), *P* = .289, Calculated RR, 1.8;	**Most common TEAE** nasopharyngitis 24.4% Ixekizumab vs. 27.1% Ustekinumab No deaths reported at 12 or 52 weeks. **Infections at 52 weeks:** 61.5% Ixekizumab vs. 64.5% Ustekinumab, *P* = .632 **Injection-site reactions at 52 weeks:** 16.3% Ixekizumab vs. 1.2% Ustekinumab, *P* ≤ .001, Calculated RR = 13.53; 95% CI, 3.2, 56.5

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			graph only) *Outcomes at 24 weeks* **PASI 75** Ixekizumab: 91.2% Ustekinumab: 89.8%, *P* ≤ .05 **PASI 90** Ixekizumab: 83.1% Ustekinumab: 59%, *P* < .001 **PASI 100** Ixekizumab: 49.3% Ustekinumab: 23.58%, *P* < .001 **EQ-5D-5L mean (SD) change** 0.119 (0.21) (ustekinumab) vs. 0.161 (0.23) (infliximab), *P* > .05 **EQ-PsO Index Score mean (SD) change** 0.121 (0.15) (ustekinumab) vs. 0.156 (0.16) (ixekizumab), *P* < .05 **EQ-5D VAS mean (SD) change** 10.72 (22.7) (ustekinumab) vs. 15.38 (22.4) (ixekizumab, *P* > .05 **WPAI-PsO change** No difference between groups (data reported in graph only) *Outcomes at 52 weeks:* **PASI 75** 89.2% (ixekizumab) vs. 76.3% (ustekinumab), *P* = .006, calculated RR, 1.2; 95% CI, 1.05 to 1.3) **PASI 90** 77.4% (Ixekizumab) vs. 59.2% (ustekinumab), *P* = .003, calculated RR, 1.3; 95% CI, 1.1 to 1.5) **PASI 100** 52.7% (ixekizumab) vs. 35.2% (ustekinumab), *P* = .014; calculated RR. 1.5; 95% CI, (1.1 to 1.9 **PGA 0 or 1** 83.6% (ixekizumab) vs. 65.8%	95% CI, 0.67 to 5.1 **% (N) withdrawal due to an AE** Ixekizumab 2.2% (3/135) vs. ustekinumab 1.2% (2/166), *P* = .66, Calculated RR. 1.8; 95% CI, 0.31 to 10.9 **Death** Ixekizumab 0% (0/135) vs. ustekinumab 0% (0/166)	

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			(ustekinumab), *P* = .002, calculated RR, 1.3; 95% CI, (1.1 to 1.4 **PGA 0** 53.5% (ixekizumab) vs. 35.8% (ustekinumab), *P* = .013; Calculated RR. 1.5; 95% CI, 1.1 to 1.9 **% Itch NRS 0** 41.2% (ixekizumab) vs. 34.3% (ustekinumab), *P* > .05 **% Itch NRS ≥ 4-point improvement** Proportions similar in both groups, data reported in graph only **Skin pain VAS mean change** -36.54 (ixekizumab) vs. −31.79 (ustekinumab), *P* > .05 Skin pain VAS 0 48.5% (ixekizumab) vs. 41% (ustekinumab, *P* > 0.5 **% DLQI 0 or 1** 71.3% (ixekizumab vs. 56.6% (ustekinumab), *P* < .01 **EQ-5D-5L mean (SD) change** 0.126 (0.22) (ustekinumab) vs. 0.16 (0.24) (ixekizumab), *P* > .05 **EQ-PsO Index Score mean (SD) change** 0.12 (0.16) (ustekinumab) vs. 0.142 (0.18) (ixekizumab), *P* > .05 **EQ-5D VAS mean (SD) change** 12.52 (22.1) (ustekinumab) vs. 13.38 (22.5) (ixekizumab), *P* > .05 **WPAI-PsO change** No difference between treatment groups (data reported in graph only) Mean change in SF-36-PCS score 5.53 (ixekizumab) vs. 3.28 (ustekinumab), *P* < .05 No significant difference in mean change in SF-36		

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			MCS score. *Subgroup analysis* Participants with nail psoriasis, N Ixekizumab: 84 Ustekinumab: 105 *Outcomes at 16 weeks* **% NAPSI 0** 31% (ixekizumab) vs. 16.2% (ustekinumab), *P* = .02 *Outcomes at 52 weeks* **% NAPSI 0** 61.9% (ixekizumab) vs. 28.6% (ustekinumab), *P* < .001 **% PASI 100** Participants with nail psoriasis: 53.6% (ixekizumab) vs. 27.6% (ustekinumab) Participants without nail psoriasis: 50% (ixekizumab) vs. 49.2% (ustekinumab)		
Ritchlin et al., 2020[20] BE ACTIVE Moderate	Placebo SC every 4 weeks for 12 weeks then reassigned to either 160 mg or 320 mg after 12 weeks until 48 weeks Bimekizumab 320 mg SC every 4 weeks for 48 weeks Only follow-up at 12 weeks is eligible for inclusion in this	Placebo: 42 Bimekizumab 16 mg: 41 Bimekizumab 160 mg: 41 Bimekizumab 160-mg loading dose: 41 Bimekizumab 320 mg: 41 Total: 206 This was a dose-ranging study; 320 mg is the dose that was used in	At 12 weeks Primary outcome N (%) ACR50 Bimekizumab 320 mg: 10 (24) Placebo: 3 (7) Reported OR (95% CI): 3.7 (1.0 to 13.7), *P* = .05 Calculated RR (95% CI): 3.4 (1.01 to 11.5), *P* = .04 Secondary outcomes N (%) ACR20 Bimekizumab 320 mg: 21 (51) Placebo: 8 (19) Reported OR (95% CI): 4.2 (1.6 to 11.4), *P* = .004 Calculated RR (95% CI): 2.7 (1.3 to 5.4), *P* = .002 N (%) ACR70 Bimekizumab 320 mg: 6 (15) Placebo: 2 (5)	At 12 weeks N (%) any TEAE Bimekizumab 320 mg: 20 (49) Placebo: 24 (57) Calculated RR (95% CI): 0.85 (0.57 to 1.3) N (%) serious TEAE Bimekizumab 320 mg: 0 (0) Placebo: 1 (2) Calculated RR (95% CI): NA (0 events in 1 arm) N (%) discontinuations due to TEAE	Serious infection 0 in both groups Mortality 0 in both groups Malignancies 0 in both groups Major cardiovascular events 0 in both groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	review.	subsequent phase 3 studies and is the only dose summarized in this update.	Reported OR (95% CI): 2.9 (0.6 to 13.4), *P* = .17 Calculated RR (95% CI): 3.1 (0.66 to 14.4), *P* = .15 N (%) MDA Bimekizumab 320 mg: 12 (29) Placebo: 6 (14) Calculated RR (95% CI): 2.0 (0.85 to 4.9), *P* = .11 Mean change (SD) from baseline in MASES Bimekizumab 320 mg: −1.0 (3.8) Placebo: −0.4 (3.5) Calculated mean difference (95% CI): −0.6 (−2.2 to 0.99), *P* = .46 N (%) PASI 90 Bimekizumab 320 mg: 14 (54) Placebo: 2 (7) Reported OR (95% CI): 12.1 (2.6 to 56.2), *P* = .001 Calculated RR (95% CI): 7.2 (1.7 to 29.6), *P* < .001 N (%) PASI 75 Bimekizumab 320 mg: 19 (73) Placebo: 2 (7) Reported OR (95% CI): 27.1 (5.6 to 131.1), *P* < .0001 Calculated RR (95% CI): 9.7 (2.4 to 39.2), *P* < .001 Mean change (SD) from baseline in HAQ-DI Bimekizumab 320 mg: −0.4 (0.5) Placebo: −0.1 (0.5) Calculated mean difference (95% CI): −0.3 (−0.52 to −0.08), *P* = .008 Mean change (SD) in SF-36 PCS score Bimekizumab 320 mg: 6.5 (8.4) Placebo: 2.7 (8.4) Calculated mean difference (95% CI): 3.8 (0.13 to 7.5), *P* = .04 Mean change (SD) in SF-36 MCS score Bimekizumab 320 mg: 1.7 (8.4)	Bimekizumab 320 mg: 0 (0) Placebo: 2 (5) Calculated RR (95% CI): NA (0 events in 1 arm) N (%) drug-related TEAE Bimekizumab 320 mg: 8 (20) Placebo: 4 (10)	

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Placebo: −1.2 (7.2) Calculated mean difference (95% CI): 2.9 (−0.51 to 6.3), *P* = .09 N (%) Psoriatic Arthritis Impact of Disease score ≤3 Bimekizumab 320 mg: 22 (54) Placebo: 12 (29) Calculated RR (95% CI): 1.9 (1.1 to 3.3), *P* = .02		
Reich et al., 2017[49] LIBERATE Moderate	Etanercept 50 mg subcutaneous twice weekly Apremilast 30 mg oral tablet twice per day Placebo Duration 16 weeks, after which there was an extension phase which is not included here	Etanercept: 83 Apremilast: 83 Placebo: 84 Total: 250	*Primary outcome at 16 weeks* **% PASI 75** 39.8% (apremilast) vs. 48.2% (etanercept), *P* = .26 (post hoc) *Secondary outcomes at 16 weeks* **% PGA 0 or 1** 21.7% (apremilast) vs. 28.9% (etanercept), *P* NR **% PASI 50** 62.7% (apremilast) vs. 83.1% (etanercept), *P* NR **Mean (SD) BSA change** −48.3 (35.1) (apremilast) vs. −56.5 (31.6) (etanercept), *P* NR **Mean (SD) DLQI change** −8.3 (7.7) (apremilast) vs. −7.8 (6.5) (etanercept) *Exploratory Outcome* **% PASI 90** 14.5% (apremilast) vs. 20.5% (etanercept), *P* NR	**% AEs** Apremilast: 71.1% Etanercept: 53.0%, *P* NR ≥ 95% of AEs were mild or moderate in severity Calculated RR, 1.3; 95% CI, 1.05 to 1.7 **% SAEs** Apremilast: 3.6% Etanercept: 2.4%, *P* NR Calculated RR, 1.5; 95% CI, 0.26 to 8.7 **% withdrawals due to AE** Apremilast: 3.6% Etanercept: 2.4%, *P* NR Calculated RR, 1.5; 95% CI, 0.26 to 8.7	Most common AEs (in ≥ 5% of participants in any treatment group): nausea, diarrhea, upper respiratory tract infection, nasopharyngitis, tension headache and headache Triglycerides > 3 .4 mmol/L: 12% apremilast, 17% etanercept, *P* NR
Warren et al., 2021[25] BE SURE	Bimekizumab 320 mg SC every 4 weeks for 56 weeks Bimekizumab 320	Bimekizumab 320 mg every 4 weeks: 158 Bimekizumab 320 mg every 4	At week 16 Primary outcomes N (%) PASI 90 Bimekizumab 320 mg: 275 (86.2) Adalimumab: 75 (47.2)	N (%) any AE Bimekizumab every 4 weeks: 112 (70.9) Bimekizumab every 4 weeks then every 8	N (%) mortality Bimekizumab every 4 weeks: 0 (0) Bimekizumab

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
Moderate	mg SC every 4 weeks for 16 weeks, then every 8 weeks for weeks 16 to 56 Adalimumab 40 mg SC every 2 weeks for 24 weeks, followed by bimekizumab 320 mg SC every 4 weeks to week 56 Only results reported through 24 weeks were included for this update.	weeks for 16 weeks then every 8 weeks: 161 Adalimumab 40 mg every 2 weeks: 159 Total: 478	Bimekizumab vs. adalimumab Reported ARD (95% CI): 39.3 (30.9 to 47.7), *P* < .001 Calculated RR (95% CI): 1.8 (1.5 to 2.2), *P* < .001 N (%) IGA 0 or 1 Bimekizumab 320 mg: 272 (85.3) Adalimumab: 91 (57.2) Bimekizumab vs. adalimumab Reported ARD (95% CI): 28.2 (19.7 to 36.7), *P* < .001 Calculated RR (95% CI): 1.5 (1.3 to 1.7), *P* < .001 Secondary outcome at week 16 N (%) PASI 100 Bimekizumab 320 mg: 194 (60.8) Adalimumab: 38 (23.9) Bimekizumab vs. adalimumab Reported ARD (95% CI): 37.0 (28.6 to 45.3), *P* < .001 Calculated RR (95% CI): 2.5 (1.9 to 3.4), *P* < .001 Secondary outcomes at week 24 N (%) PASI 100 Bimekizumab every 4 or 8 weeks: 213 (66.8) Adalimumab: 47 (29.6) Reported ARD (95% CI): 37.1 (28.5 to 45.7), *P* < .001 Calculated RR (95% CI): 2.3 (1.8 to 2.9), *P* < .001 Bimekizumab every 4 weeks: 107 Reported ARD (95% CI): 37.9 (28.1 to 47.7) Calculated RR (95% CI): 2.3 (1.8 to 3.0), *P* < .001 N (%) PASI 90 Bimekizumab every 4 or 8 weeks: 273 (85.6) Adalimumab: 82 (51.6) Reported ARD (95% CI): 33.9 (25.4 to 42.4), *P* < .001 Calculated RR (95% CI): 1.7 (1.4 to 1.9), *P* < .001	weeks: 116 (72.0) Adalimumab: 111 (69.8) Calculated RR (95% CI) Bimekizumab every 4 weeks: 1.01 (0.88 to 1.2), *P* = .84 Bimekizumab every 4 weeks then every 8 weeks: 1.03 (0.90 to 1.2), *P* = .66 N (%) SAE Bimekizumab every 4 weeks: 4 (2.5) Bimekizumab every 4 weeks then every 8 weeks: 1 (0.6) Adalimumab: 5 (3.1) Calculated RR (95% CI) Bimekizumab every 4 weeks: 0.81 (0.22 to 2.9), *P* = 0.76 Bimekizumab every 4 weeks then every 8 weeks: 0.20 (0.02 to 1.7), *P* = .12 N (%) discontinuations due to AE Bimekizumab every 4 weeks: 3 (1.9) Bimekizumab every 4 weeks then every 8 weeks: 6 (3.7) Adalimumab: 5 (3.1) Calculated RR (95% CI)	every 4 weeks then every 8 weeks: 0 (0) Adalimumab: 1 (0.6) N (%) serious infections Bimekizumab every 4 weeks: 0 (0) Bimekizumab every 4 weeks then every 8 weeks: 1 (0.6) Adalimumab: 1 (0.6) N (%) cancer Bimekizumab every 4 weeks: 0 (0) Bimekizumab every 4 weeks then every 8 weeks: 4 (2.5) Adalimumab: 1 (0.6) Adjudicated major adverse cardiovascular events 0 in all groups

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
			Bimekizumab every 4 weeks: 136 (86.1) Reported ARD (95% CI): 34.3 (25.2 to 43.5) Calculated RR (95% CI): 1.7 (1.4 to 2.0), *P* < .001 N (%) IGA 0 or 1 Bimekizumab every 4 or 8 weeks: 276 (86.5) Adalimumab: 92 (57.9) Reported ARD (95% CI): 28.7 (20.2 to 37.1), *P* < .001 Calculated RR (95% CI): 1.5 (1.3 to 1.7), *P* < .001 Bimekizumab every 4 weeks: 136 (86.1) Reported ARD (95% CI): 28.3 (19.1 to 37.5) Calculated RR (95% CI): 1.5 (1.3 to 1.7), *P* < .001 N (%) DLQI 0 or 1 Bimekizumab every 4 or 8 weeks: 214 (67.1) Adalimumab: 76 (47.8) Calculated ARD (95% CI): 19.3 (10.0 to 28.6) Calculated RR (95% CI): 1.4 (1.2 to 1.7)	Bimekizumab every 4 weeks: 0.60 (0.15 to 2.5), *P* = .51 Bimekizumab every 4 weeks then every 8 weeks: 1.2 (0.37 to 3.8), *P* = .79 N (%) drug-related AE Bimekizumab every 4 weeks: 41 (25.9) Bimekizumab every 4 weeks then every 8 weeks: 46 (28.6) Adalimumab: 38 (23.9)	
Warren et al., 2021[19] IMMerge Moderate	Risankizumab administered as 2 subcutaneous injections of 75 mg (150 mg total) at weeks 0 and 4 then every 12 weeks for 40 weeks except for patients in France who received additional doses at weeks 52 and 64 Secukinumab administered as 2 subcutaneous injections of 150	Risankizumab: 164 Secukinumab: 163 Total: 327	Primary outcomes At week 16 N (%) PASI 90 Risankizumab: 121 (73.8) Secukinumab: 107 (65.6) ARD (96.25% CI): 8.2% (−2.2 to 18.6) (within the 12% noninferiority margin) At week 52 N (%) PASI 90 Risankizumab: 142 (86.6) Secukinumab: 93 (57.1) ARD (95% CI): 29.8 (20.8 to 38.8), *P* < .001 Secondary outcomes at week 52 N (%) PASI 100 Risankizumab: 108 (65.9) Secukinumab: 65 (39.9) ARD (95% CI): 26.2% (15.9 to 36.5), *P* < .001 N (%) sPGA 0/1	N (%) TEAE Risankizumab: 117 (71.3) Secukinumab: 116 (71.2) Calculated RR (95% CI): 1.00 (0.87 to 1.2) N (%) SAE Risankizumab: 9 (5.5) Secukinumab: 6 (3.7) Calculated RR (95% CI): 1.5 (0.54 to 4.1) N(%) discontinuation due to AE Risankizumab: 2 (1.2) Secukinumab: 8 (4.9) Calculated RR (95% CI): 0.25 (0.05 to 1.2)	N (%) major adverse cardiovascular event Risankizumab: 2 (1.2) Secukinumab: 0 (0) N (%) serious infection Risankizumab: 3 (1.8) Secukinumab: 0 (0) Mortality 0 in all groups N (%) malignant tumors

Author, Year Trial Name Risk of Bias	Interventions	N	Efficacy/Effectiveness Outcomes	AE General	AE Specific
	mg (300 mg total) at weeks 0, 1, 2, 3, and 4 then every 4 weeks for 48 weeks		Risankizumab: 144 (87.8) Secukinumab: 95 (58.3) ARD (95% CI): 29.8% (20.9 to 38.8), *P* < .001 N (%) PASI 75 Risankizumab: 147 (89.6) Secukinumab: 114 (69.9) ARD (95% CI): 20.0% (11.7 to 28.3), *P* < .001		Risankizumab: 1 (0.6) Secukinumab: 3 (1.8)

Notes. An asterisk (*) indicates a calculated value. [a] After 160-mg initial dose. [b] The ixekizumab group was administered a starting dose of 160 mg given as 2 injections at week 0.

Abbreviations. A2: Amagine-2 study; A3: Amagine-3 study; ACR: American College of Rheumatology percentage improvement; AE: adverse event; AMD: absolute mean difference; ARD: absolute risk difference; BMI: body mass index; BMS: Bristol-Myers Squibb; BSA: body surface area; cDMARD: conventional disease-modifying antirheumatic drugs; CI: confidence interval; COX-2: cyclooxygenase-2; DAS-CRP: Disease Activity Score including C-reactive protein; DLQI: Dermatology Life Quality Index; DMARD: disease-modifying antirheumatic drug; EQ-5D: European QoL 5-item measure of health utility; EQ-PsO: version of the EQ-5D specific to psoriasis; EQ-VAS: European QoL-Visual Analog Scale; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; GPSS: Genital Psoriasis Symptom Scale; HADS-A/HADS-D: Hospital Anxiety or Depression Scale; HAQ: Health Assessment Questionnaire; HAQ-DI: Health Assessment Questionnaire–Disability Index; IGA: Investigator's Global Assessment; IQR: interquartile range; IV: intravenous; ISI: Itch Severity Index; LDI: Leeds Dactylitis Index; LDI-B: Leeds Dactylitis Index—Basic; LEI: Leeds Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; mCPDAI: modified Composite Measures of Disease Activity in Psoriatic Arthritis; MICD: minimally important clinical difference; MDA: Minimal Disease Activity; NA: not applicable; NAPSI: Nail Psoriasis Severity Index; NCT: US National Clinical Trial; NR: not reported; NRS: Numeric Rating Scale; NS: not statistically significant as reported by study authors; NSAID: nonsteroidal inflammatory drug; OR: odds ratio; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PtGA: Patient's Global Assessment; PGA: Physician's Global Assessment; PRO: patient-reported outcomes; PsARC: Psoriatic Arthritis Response criteria; P-SIM: Psoriasis Symptoms and Impacts Measure; PSS: Psoriasis Symptom Scale; PsO: Psoriasis; PSSD: Psoriasis Symptoms and Signs Diary; PtGA: Patient's Global Assessment; PtGA-VAS; patient global assessment visual analog scale; QoL: quality of life; RCT: randomized controlled trial; RR: risk ratio; SAE: serious adverse event; SC: subcutaneous; SD: standard deviation; SE: standard error; SF-36 MCS: Short Form Survey Mental Health Component Score; SF-36 PCS: Short Form Survey Physical Health Component Score; sIGA; static Investigator Global Assessment; SJC: swollen joint count; SPARCC EI: Spondyloarthritis Research Consortium of Canada Enthesitis Index; sPGA: Static Physicians Global Assessment; TEAE: treatment-emergent adverse event; TIM: targeted immune modulator; TJC: tender joint count: TNF-α: tumor necrosis factor alpha; U2: Uncover-2 study; U3: Uncover-3 study; VAS: visual analog scale; vs.: versus; wk: weeks; WLQ: Work Limitations Questionnaire; WPAI-PSO: Work Productivity and Activity Impairment Questionnaire-Psoriasis.

Table B3. Evidence Table for Cohort Studies of TIMs in Plaque Psoriasis and Psoriatic Arthritis

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
Dommasch et al., 2019[59] US Moderate	Methotrexate Adalimumab Acitretin Apremilast Etanercept Infliximab Ustekinumab Study was conducted from January 1, 2003 to September 30, 2017.	Insurance beneficiaries within the Optum Clinformatics Data Mart between January 1, 2004 to September 30, 2017 and Truven MarketScan between January 1, 2003 to January 1, 2017. Outcomes based on ICD-9-CM codes. Serious infection defined as primary inpatient diagnosis code for pneumonia, meningitis/encephalitis, bacteremia/sepsis, cellulitis, soft-tissue infection, endocarditis, pyelonephritis, and septic arthritis/osteoarthritis.	*Optum Clinformatics Data Mart* Methotrexate: N = 8,470 Adalimumab: 7,181 Acitretin: N = 2,726 Apremilast: N = 1,623 Etanercept: N = 7,102 Infliximab: N = 408 Ustekinumab: 4,085 Total: N = 31, 585 *Truven MarketScan* Methotrexate: 20,609 Adalimumab: N = 17,912 Acitretin: N = 7,456 Apremilast: N = 4,476 Etanercept: N = 16,791 Infliximab:	Psoriasis participants with at least 3 ICD-9-CM codes of 696.1 on separate dates. Participants were included if they had a prescription claim for acitretin, adalimumab, apremilast, etanercept, infliximab, ustekinumab, or methotrexate. Participants were required to have continuous medical and prescription coverage during the 180 days prior to and on the cohort entry data. Participants were excluded if they had a claim for any study drug during the 180 days prior to the cohort entry date, were younger than 18 years, or a prescription for the index study drug with day supply of 0. If patient had 1 of the following within 180 days of the cohort entry date the participant was excluded, a claim for more than 1 systemic medication for psoriasis	**Serious infection requiring hospitalization** HR, 95% CI (vs. adalimumab) Apremilast: 0.31, 0.15 to 0.65 Etanercept: 0.76, 0.61 to 0.94 Infliximab: 1.92,1.01 to 3.62 Ustekinumab: 0.70, 0.49 to 1.00	The Division of Pharmaco-epidemiology and Pharmaco-economics, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
			N = 1,027 Ustekinumab: N = 7,841 Total: N = 76,112	or other immunosuppressive medications, history of any malignancy, history of any serious infection, or a diagnosis of another immune mediated inflammatory disorder for which biologics may be used. Mean age: varied from 46 to 53across agents N (%) female: 51,008(47.3)		
Jin et al., 2021[27] US Moderate	Ustekinumab, adalimumab, apremilast, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, secukinumab; doses as prescribed in usual care. Duration of exposure only reported in aggregate as cumulative person-years.	Sample identified from 2 US claims databases. MarketScan September 2009 through December 2017 and Optum September 2009 through December 2018. Persons identified based on diagnosis codes for plaque psoriasis or psoriatic arthritis, with initial pharmacy claim for any of the 9 drugs evaluated in this analysis.	MarketScan Database Adalimumab: 28,484 Apremilast: 9,145 Certolizumab pegol: 1,189 Etanercept: 17,850 Golimumab: 1,585 Infliximab: 4,017 Ixekizumab: 1,299 Secukinumab: 3,861 Ustekinumab: 13,448	Persons age 18 years or older with at least 2 inpatient or outpatient diagnosis codes of plaque psoriasis or psoriatic arthritis (ICD-9 CM/10) during a 6-month baseline period and continuously enrolled with insurance for at least 6 months prior to the index date. Participants with serious infection in prior 60 days, rheumatoid arthritis, inflammatory bowel disease, malignancy, HIV, or organ transplant were excluded. Across the 9 drugs and 2 databases:	Hospitalization for serious infection, vs. ustekinumab adjusted HR (95% CI) Adalimumab: 1.66 (1.34 to 2.06) Apremilast: 1.42 (1.02 to 1.96) Certolizumab pegol: 1.09 (0.68 to 1.75) Etanercept: 1.39 (1.01 to 1.90) Golimumab: 1.74 (1.00 to 3.03) Infliximab: 2.92 (1.80 to 4.72) Ixekizumab: 2.98 (1.20 to 7.41) Secukinumab: 1.84 (1.24 to 2.72)	Division of Pharmaco-epidemiology and Pharmaco-economics at Brigham and Women's Hospital

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
			Optum Database: Adalimumab: 13,768 Apremilast: 5,766 Certolizumab pegol: 989 Etanercept: 7,588 Golimumab: 1,164 Infliximab: 1,348 Ixekizumab: 661 Secukinumab: 2,990 Ustekinumab: 8,231	Mean age range: 46.8 to 53.3 % female range: 46.8 to 63.7 % with plaque psoriasis only range: 4.8 to 85.4 % with psoriatic arthritis-only range: 1.8 to 69.6 % with history of cDMARDS range: 19.8 to 75.8 % with history of bDMARDS range: 15.0 to 47.7		
Kisacik et al., 2016[56] Turkey High	Infliximab Etanercept Adalimumab	September 2002 to 2012	N = 10,434 (7,695 used) Infliximab: N = 2,684 (without TB), N = 46 with Adalimumab: N = 2,238 (without), N = 14 with Etanercept: N = 2,773 (without), N = 13 (with)	Participants from member centers of the Turkish Multicentered Investigators Platform in Rheumatology Mean age (SD): 43.4 (13.6) without TB, 43.6 (13) with Gender: N = 3,634 males/4,061 females without, N = 39 males/34 females with	**Incidence of TB** Infliximab (1.27%) Etanercept (0.30%) and adalimumab (0.57%) *P* < .001 and *P* = .008, respectively vs. infliximab Adalimumab vs. etanercept, *P* = .08	NR

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
Lee et al., 2019[58] US Moderate	Ustekinumab (dose unspecified) TNF-α inhibitors (specifically adalimumab, etanercept, infliximab, certoliz-umab, or golimumab) Mean (SD) follow-up: 1.4 (1.3) years, Maximum follow-up: 6 years	Adults between September 25, 2009, and September 30, 2015. Data were acquired from Optum and MarketScan databases, which contain a nationwide sample of commercially insured participants.	Ustekinumab: N = 9,071 TNF-α inhibitors: N = 50,957 Total: N = 60,028	Adults with at least 1 visit coded for psoriasis or psoriatic arthritis who initiated therapy with ustekinumab or a TNF-α inhibitor (i.e., adalimumab, etanercept, infliximab, certolizumab, or golimumab) with at least 12 months of continuous enrollment in the health plan before the index date. The cohort entry date (i.e., index date) was defined as the date of ustekinumab or TNF-α inhibitor therapy initiation, and treatment initiation was defined as the absence of the pertinent drug exposure within the last 12 months of the index date. Participants who had a previous diagnosis of atrial fibrillation (ICD-9-CM diagnosis code 427.3x) or received antiarrhythmic or anticoagulant therapy during the baseline period. N (%) male: 29,495 (49.1%)	**N incident atrial fibrillation** Ustekinumab: 60 Anti-TNF-α: 323 adjusted HR, 1.08; 95% CI, 0.76 to 1.54 for ustekinumab vs. anti-TNF-α **N incident major cardiovascular event** Ustekinumab: 74 Anti-TNF-α: 421 adjusted HR,1.10; 95% CI, 0.80 to 1.52 for ustekinumab vs. anti-TNF-α	Division of Pharmaco-epidemiology and Pharmaco-economics at the Brigham and Women's Hospital

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
				Mean Age (SD) Ustekinumab (Optum cohort): 46.0 (12.6) Ustekinumab (MarketScan cohort): 46.7 (12.9) TNF-α inhibitor (Optum cohort): 47.3 (13.0) TNF-α inhibitor (MarketScan cohort): 47.3 (12.6)		
Li et al., 2020[30] US Moderate	Three mutually exclusive exposures: IL-17 (ixekizumab or secukinumab) IL-12/23 (ustekinumab) TNF-α (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) Exposure defined based on pharmacy claims data;	Beneficiaries with claims within OptumLabs data sources between January 1, 2015, and May 1, 2018. This data source represents over 100 million individuals in all 50 states of all ages and ethnic groups. Persons with at least 1 ICD-9-CM diagnosis code prior to the index date for psoriasis (code 696.1 or ICD-10-CM code L40.9) or psoriatic arthritis (ICD-9-CM code 696.0; ICD-10-CM codes L40.50,	Number of treatment episodes IL-17: 2,148 IL-12/23: 2,882 TNF-α: 6,530 Total: 11,560 treatment episodes from 9,305 persons	Adults with diagnosis code for psoriasis or psoriatic arthritis in claims data with prescription dispensation or medical infusion for biologics of interest between January 2015 and May 2018. Persons with rheumatoid arthritis, Crohn's disease, ulcerative colitis, osteoarthritis, HIV, cancer, leukemia, lymphoma during 24 months prior to index date were excluded as were persons with a serious infection in the 60 days prior to the index date. Mean (SD) age: 46 (12) N (%) female: 5,453 (47%)	N (%) serious infections; incidence rate per 100 person-years (95% CI) Anti-IL-17: 32 (1); 2.1 (1.5 to 2.9) Anti-IL 12/23: 32 (1); 1.3 (0.9 to 1.8) Anti-TNF-α: 126 (2); 2.4 (2.0 to 2.8) Adjusted HR (95% CI) for first serious infection Anti-IL-17 vs. anti-TNF-α: 0.89 (0.48 to 1.66) Anti-IL-12/23 vs. anti-TNF-α: 0.59 (0.39 to 0.90) Anti-IL-17 vs. anti-IL – 12/23: 1.12 (0.62 to 2.03) Consistent results in the psoriasis only group; no significant	Center for Drug Safety and Effectiveness at the Johns Hopkins Bloomberg School of Public Health

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
	no dosages specified and duration assigned based on typical dosage regimen.	L40.51, L40.52, L40.53, L40.54, L40.59) from a dermatologist or rheumatologist visit were included. Serious infection defined as claim for hospitalization with infection listed in primary or nonprimary diagnosis position. Subjects followed until first hospitalization or were censored if they developed an excludable condition, discontinued therapy (switch or treatment gap of 90 days), lost enrollment, or died.		Psoriasis only: 6,043 (52%) Psoriatic arthritis only: 1,869 (16%) Both: 3,648 (32%) N (%) White: 9,161 (79%) N (%) Black: 728 (6) N (%) Hispanic: 1,215 (11%) N (%) Asian: 456 (4%)	differences among agents in the psoriatic arthritis-only group.	

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
Munera-Campos et al., 2021[29] Spain High	Anti-IL 23, anti-IL 17, apremilast, anti-TNF-α, doses and mean duration of treatment not reported and specific drugs were not reported.	Eligible persons selected from BIOBADADERM registry between January 2008 and November 2019. AEs coded according to Medical Dictionary for Regulatory Activities (MedDRA). All AEs requiring a medical consultation or change of dose are included in the registry.	Number of person-years of exposure Anti-IL 23: 2,775 Anti-IL 17: 845 Apremilast: 251 Anti-TNF-α: 4,280 Total	Persons with psoriasis registered on the BIOBADADERM registry receiving modern therapy. The registry covers 18 Spanish hospitals. Persons receiving combination therapy were excluded. Across agents included: Mean age range: 50 to 57 years % female range: 40 to 61 % with psoriatic arthritis range: 12 to 18 Mean duration of disease range: 19 to 20 years	Liver test abnormalities; incidence per 1,000 person-years (95% CI); adjusted IRR vs. anti-TNF-α Anti-IL 23: 11 (8 to 15); 0.78 (0.33 to 1.83) Anti-IL 17: 5 (2 to 13); 0.65 (0.19 to 2.19) Apremilast: 0; NA Anti-TNF-α: 17 (13 to 21); NA Nonalcoholic fatty liver disease Anti-IL 23: 10 (7 to 14); 2.16 (0.71 to 6.54) Anti-IL 17: 12 (6 to 22); 4.16 (1.36 to 12.7) Apremilast: 0; NA Anti-TNF-α: 7 (5 to 10); NA All hepatic AEs Anti-IL 23: 25 (20 to 32); 1.15 (0.64 to 2.08) Anti-IL-17: 20 (13 to 32); 1.46 (0.75 to 2.85) Apremilast: 0; NA Anti-TNF-α: 32 (27 to 38); NA	Fundacion Piel Sana Academia Espanola de Dermatologica y Venereologia, Spanish Medicines and Health Products Agency, pharma-ceutical companies
Penso et al., 2021[28] France Moderate	Doses of drugs not specified. Treatment exposure	Participants identified through French national Health Data System covering 65 million	Total: 44,239 Adalimumab: 15,925 (36.0%)	Adults registered in French national health data systems (covering 98.8% of the population) identified as having	N (%) serious infections, incidence rate per 1,000 person-years (95% CI) and adjusted	NR

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
	were identified in national health databases by Anatomical Therapeutic Chemical Codes. Exposure was defined as time from initiation to discontinuation, which was at least 90 days without completion of a a prescription for the same biologic. Only exposure to a first biologic was included in the analysis. Median follow-up (IQR) in months Adalimumab: 13 (7 to 26)	persons (98.8%) of the population linked to national hospital discharge database. Eligible adults with psoriasis prescribed first biologic agent between January 1, 2009 and July 31, 2019 were included. Outcomes were defined as first occurrence of serious infection after the index date, defined based on presence of ICD-10 codes for gastrointestinal, cutaneous, eyes, ear-nose-throat, musculoskeletal, pulmonary, nervous system, and other infections in national health databases.	Apremilast: 3,344 (7.6%) Brodalumab: 180 (0.4%) Certolizumab pegol: 1,030 (2.3%) Etanercept: 9,661 (21.8%) Guselkumab: 526 (1.2%) Infliximab: 3,002 (6.8%) Ixekizumab: 768 (1.7%) Secukinumab: 3,145 (7.1%) Ustekinumab: 6,658 (15.1%)	psoriasis based on at least 2 prescriptions for topical vitamin D derivatives (considered first-line treatment in France) who were new users of a biologic agent or apremilast between January 1, 2009 and July 31, 2019. New users were defined as no prescription in the year prior to the index date, which was the date of fulfillment of prescription for biologic agent. Persons with HIV, history of cancer, transplant, or serious infection within 2 years prior to the index date were excluded. Mean (SD) age: 48.4 (13.8) N (%) female: 21,373 (48.3) N(%) with psoriatic arthritis: 5,102 (11.5)	HR (95% CI) vs. etanercept Adalimumab: 697 (4.4); 27.2 (25.7 to 29.8); 1.22 (1.07 to 1.38) Apremilast: 64 (1.9); 21.7 (16.4 to 27); 0.83 (0.63 to 1.10) Brodalumab: 2 (1.1); 17.8 (0 to 42.4); 0.79 (0.21 to 2.95) Certolizumab pegol: 35 (3.4); 26.7 (17.9 to 35.6); 1.15 (0.83 to 1.59) Etanercept: 367 (3.8); 24.8 (22.3 to 27.4); referent Guselkumab: 8 (1.5); 29.9 (9.2 to 50.7); 1.37 (0.70 to 2.67) Infliximab: 171 (5.7); 43 (36.5 to 49.4); 1.79 (1.49 to 2.16) Ixekizumab: 15 (2.0); 17.7 (8.8 to 26.7); 0.82 (0.50 to 1.35) Secukinumab: 95 (3.0); 21.9 (17.5 to 26.3); 0.94 (0.74 to 1.18) Ustekinumab: 202 (3.0); 16.3 (14 to 18.5); 0.79 (0.67 to 0.94)	

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
	Apremilast: 7 (4 to 14) Brodalumab: 7 (4 to 11) Certolizumab pegol: 9 (6 to 19) Etanercept: 12 (7 to 25) Guselkumab: 6 (3 to 9) Infliximab: 12 (10 to 13) Ixekizumab: 11 (6 to 19) Secukinumab: 13 (7 to 25) Ustekinumab: 17 (10 to 31)				In a sensitivity analysis using competing risks, pairwise comparisons done between all agents. The following pairwise comparisons were statistically significant: Weighted subhazard ratio (95% CI) vs. adalimumab Apremilast 0.68 (0.52 to 0.89) Brodalumab 0.65 (0.18 to 2.42) Certolizumab 0.94 (0.69 to 1.30) Etanercept 0.82 (0.72 to 0.93) Guselkumab 1.12 (0.58 to 2.18) Infliximab 1.47 (1.24 to 1.74) Ixekizumab 0.67 (0.41 to 1.11) Secukinumab 0.77 (0.62 to 0.96) Ustekinumab 0.65 (0.56 to 0.76) vs. apremilast Brodalumab 0.95 (0.25 to 3.63) Certolizumab 1.38 (0.92 to 2.07)	

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
					Guselkumab 1.64 (0.81 to 3.34) Infliximab 2.16 (1.59 to 2.92) Ixekizumab 0.99 (0.57 to 1.72) Secukinumab 1.14 (0.82 to 1.58) Ustekinumab 0.95 (0.71 to 1.28) vs. guselkumab Brodalumab 0.58 (0.13 to 2.52) Certolizumab 0.84 (0.41 to 1.75) Infliximab 1.31 (0.67 to 2.58) Ixekizumab 0.60 (0.26 to 1.37) Secukinumab 0.69 (0.35 to 1.38) Ustekinumab 0.58 (0.30 to 1.14) vs. Infliximab Brodalumab 0.44 (0.12 to 1.66) Certolizumab pegol 0.64 (0.46 to 0.91) Ixekizumab 0.46 (0.27 to 0.77) Secukinumab 0.53 (0.41 to 0.68) Ustekinumab 0.44 (0.36 to 0.54)	

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
					vs. brodalumab Certolizumab 1.45 (0.38 to 5.58) Ixekizumab 1.03 (0.26 to 4.19) Secukinumab 1.19 (0.32 to 4.48) Ustekinumab 1.00 (0.27 to 3.74) vs. Certolizumab Ixekizumab 0.71 (0.40 to 1.28) Secukinumab 0.82 (0.57 to 1.19) Ustekinumab 0.69 (0.49 to 0.97) vs. ixekizumab Secukinumab 1.15 (0.68 to 1.96) Ustekinumab 0.97 (0.58 to 1.61) vs. secukinumab Ustekinumab 0.84 (0.66 to 1.07)	
Rungapiromnan et al., 2020[32] UK and Republic of Ireland Moderate	Ustekinumab (dose unspecified): 1.76 years (IQR 0.92 to 2.96) Etanercept or adalimumab (dose unspecified):	BADBIR, a prospective registry for participants with psoriasis treated at 160 dermatology centers in UK and Republic of Ireland; participants were prospectively	Total: 5,468 Ustekinumab: 951 TNF-α: 4,517	Adults with moderate-to-severe psoriasis enrolled in the prospective BADBIR between September 2007 and October 2016 with at least 6 months of follow-up data. Participants were naïve to biologic therapies. Participants	Number of major cardiovascular events; incidence per 1,000 patient-years (95% CI) Ustekinumab: 7; 3.61 (1.72 to 7.58) TNF-α: 24; 2.46 (1.65 to 3.67)	National Institute for Health Research; multiple pharma companies provide funding to the British Association of

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
	1.69 years (IQR 0.81 to 3.10)	enrolled with information provided by providers and participants and follow-up data collected every 6 months for the first 3 years and then annually. Patient deaths are ascertained through linkage with the Office of National Statistics mortality records. Outcomes of interest (fatal or nonfatal major cardiovascular events) included acute coronary syndrome, unstable angina, myocardial infarction, or stroke. Study authors confirmed all events coded in the registry with study sites. Participants were followed until first event, change in treatment, end of		with a history of major cardiovascular events were excluded. Mean age Ustekinumab: 45 (range 35 to 54) TNF-α: 44 (range 35.2 to 53) N (%) female Ustekinumab: 361 (38) TNF-α: 1,872 (41%) N (%) White Ustekinumab: 853 (89.7) TNF-α: 4,157 (92.2) PASI score Ustekinumab: 14.6 (range 11.2 to 19.2) TNF-α: 14.1 (range 11.0 to 19.3) Concurrent psoriatic arthritis Ustekinumab: 134 (14.1) TNF-α: 1,035 (22.9)	Adjusted IRR ustekinumab vs. TNF-α: 1.47 (0.53 to 3.52) Adjusted IRR ustekinumab vs. adalimumab: 1.30 (0.46 to 3.24) Adjusted IRR etanercept vs. adalimumab: 0.62 (0.18 to 1.72)	Derm-atologists to support the BADBIR registry

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
		recorded data in the registry, death, or end of study follow-up (September 2016).				
Srinivas et al., 2020[31] Sweden Moderate	Secukinumab (dose not specified) duration no more than 2 years Ustekinumab (dose not specified) duration no more than 9 years	Cohort study involving linkage of data from multiple national registers including: National Patient Register (NPR), Swedish Prescribed Drug Register, Swedish Cancer Register, Cause of Death Register, and population registers. Outcomes identified from NPR and include respiratory infection, urinary tract infection, and candidiasis.	Total: 1,955 Secukinumab: 848 (43%) Ustekinumab: 1,107 (57%)	All individuals registered in the period 1964 to 2013 with diagnosis codes for psoriasis and psoriatic arthritis coded using ICD-10: L40, M070, M073 (from 1997); ICD-9:696,713D; ICD-8:696; ICD-7:706. All individuals were new users of secukinumab (between 2015 and 2017) or were new users of ustekinumab between 2009 and 2017. Age ≥50 years Secukinumab:451 (53%) Ustekinumab: 556 (50%) N (%) female Secukinumab: 439 (52%) Ustekinumab: 503 (45%)	Crude IR (95% CI) antibiotics for RTI and UTI per 1,000 person-days Secukinumab: 1.10 (0.98 to 1.24) Ustekinumab: 0.61 (0.56 to 0.66) Adjusted HR (95% CI): 1.22 (1.03 to 1.43) Crude IR (95% CI) Severe RTI and UTI per 1,000 person-days Secukinumab: 0.07 (0.05 to 0.11) Ustekinumab: 0.06 (0.05 to 0.07) Adjusted HR (95% CI): 0.96 (0.57 to 1.61) Crude IR (95% CI) Candidiasis per 1,000 person-days Secukinumab: 0.04 (0.02 to 0.07) Ustekinumab: 0.02 (0.01 to 0.03) Adjusted HR (95% CI): 1.80 (0.84 to 3.84)	None

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
Warren et al., 2015[55] 2015 UK Moderate	Adalimumab Etanercept Infliximab Ustekinumab Dose and duration of exposure NR	2007-2014 BAD Biologic Interventions Register	Adalimumab: 1,879 Etanercept: 1,098 Infliximab: 96 Ustekinumab: 450 Total: 3,523	Biologically naïve participants with chronic plaque psoriasis. Mean (SD) Age: 45.3 (12.8) years Disease duration: 22.0 (12.4) years Age of onset: 23.3 (12.9) years 39.7% female. BMI 31.1 kg/m^2 (7.3) Overall, 60.9% of participants had 1 or more comorbidities (hypertension (27.7%), depression (23.3%), and psoriatic arthritis (20.1%) being the most common).	**Withdrawal due to AEs** Compared with adalimumab: Etanercept: RR, 0.77; 95% CI, 0.58 to 1.02 Infliximab: RR, 2.82; 95% CI, 1.79 to 4.45; *P* < .05 Ustekinumab: RR, 0.60; 95% CI, 0.39 to 0.92	BAD receives income from by AbbVie, Janssen Cilag, Novartis, Samsung Bioepis, Eli Lilly, and Pfizer for providing pharmacovigilance services.
Wu et al., 2018[57] US Moderate	Dose not reported Mean (SD) duration in months: Adalimumab: 11.0 (7.5) Etanercept: 11.9 (11.3) Ustekinumab: 8.3 (8.5) Infliximab: NR	Adults with claims between September 1, 2008 and September 30, 2015. Data acquired from the Truven Health Analytics MarketScan Commercial Claims and Encounters database, a large US administrative claims database. AEs were defined based on FDA	Overall: 10,065 Adalimumab: 5,197 Other biologic agents: 4,868 Etanercept: 3,311 Ustekinumab: 1,370 Infliximab: 187	Adults who were biologic-naïve with ≥ 2 psoriasis diagnoses on claims, with at least 1 recorded during a dermatologist encounter. Inclusion based on (1) continuous health care plan enrollment during the baseline period and ≥1 month after the index date, (2) ≥2 prescription fills, administrations, or sessions for ≥1 of the studied biologics, and (3) were initiated on their	There were no statistically significant differences in the risk of adverse medical conditions between participants treated with adalimumab and other biologic therapies. Adjusted HR, (95% CI), *P* value Abnormal lab results: 0.96 (0.85 to 1.09); .57 Infection: 1.02 (0.96 to 1.08); .57 Mental disorder: 1.03 (0.93 to 1.13); .59	AbbVie

Author, Year Country Risk of Bias	Drug Dosage Duration of Exposure	Sample Time Frame, Data Source	Sample Size	Population Characteristics	Harms	Funder
		labels, postmarketing surveillance registries, and included abnormal lab results, infections, metal disorders, cardiovascular disease, malignancies, and respiratory disease. Only medical claims recorded during an inpatient or emergency department visit were considered for cardiovascular and respiratory conditions.		index treatment in monotherapy. The index date was defined as the initiation date of the first biologic therapy. Median age Adalimumab: 46 years Etanercept: 46 years Ustekinumab: 47 years Infliximab: NR % female Adalimumab: 47.0 Etanercept: 48.4 Ustekinumab: 46.2% Infliximab: NR	Cardiovascular disease: 1.14 (0.95 to 1.35); .15 Malignancy: 0.87 (0.67 to 1.13); .29 Respiratory disease: 1.23 (0.99 to 1.54); .06	

Abbreviations. AE: adverse event; BAD: British Association of Dermatologists; BMI: body mass index; cDMARD: conventional disease-modifying antirheumatic drug; CI: confidence intervals; FDA: US Food and Drug Administration; HIV: human immunodeficiency virus; HR: hazard ratio; ICD-9: international classification of disease-9th revision; IL: interleukin; IQR: interquartile range; IR: incidence rate; IRR: incidence rate ratio; IV: intravenous; NA: not applicable; NR: not reported; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); RoB: risk of bias; RR: risk ratio; SD: standard deviation; TB: tuberculosis; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha; UK: United Kingdom; US: United States; vs.: versus.

Appendix C. Evidence Grade Profiles

Table C1. Evidence Profile of Comparisons of TIMs for Treatment of Plaque Psoriasis

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Apremilast vs. adalimumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[28,59]/126,346	Cohort	Moderate	Consistent	Indirect	Imprecise	HR, 0.31; 95% CI, 0.15 to 0.65 Adjusted HR, 0.68; 95% CI, 0.52 to 0.89	Very low[a]
Apremilast vs. brodalumab							
Serious infection							
1 study[28]/3,524	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.05; 95% CI, 0.28 to 4.0	Very low[a]
Apremilast vs. certolizumab pegol							
Serious infection							
1 study[28]/4,374	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.72; 95% CI, 0.48 to 1.09	Very low[a]
Apremilast vs. etanercept							
Clinical improvement at 16 weeks (PASI 75)							
1 study[49]/166	RCT	Moderate	NA	Direct	Imprecise	40% vs. 48%; post hoc (*P* = .26); similar findings on secondary remission and clinical improvement endpoints	Low[b]
QoL at 16 weeks (DLQI change)							
1 study[49]/166	RCT	Moderate	NA	Direct	Imprecise	Mean (SD): −8.3 (7.7) vs. −7.8 (6.5); *P*, NR	Low[b]
Adverse events							
1 study[49]/166	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.3; 95% CI, 1.05 to 1.7	Low[b]
Serious adverse events							
1 study[49]/166	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.5; 95% CI, 0.26 to 8.7	Very low[c]
Serious infection							
1 study[28]/13,005	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.83, 95% CI, 0.63 to 1.10	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Apremilast vs. guselkumab							
Serious infection							
1 study[28]/3,870	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.61; 95% CI, 0.30 to 1.23	Very low[a]
Apremilast vs. infliximab							
Serious infection							
1 study[28]/6,346	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.46; 95% CI, 0.34 to 0.63	Very low[a]
Apremilast vs. ixekizumab							
Serious infection							
1 study[28]/4,112	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.01; 95% CI, 0.58 to 1.75	Very low[a]
Apremilast vs. secukinumab							
Serious infection							
1 study[28]/6,489	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.88; 95% CI, 0.63 to 1.22	Very low[a]
Apremilast vs. ustekinumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/46,592	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 1.42; 95% CI, 1.02 to 1.96 Adjusted HR, 1.05; 95% CI, 0.78 to 1.41	Very low[a]
Apremilast vs. anti-TNF-α							
Hepatic adverse events							
1 study[29]/4,531	Cohort	High	NA	Direct	Imprecise	Adjusted HR cannot be determined as there were 0 events in the apremilast groups.	Very low[d]
Bimekizumab (pipeline drug) vs. adalimumab							
Disease remission at 16 to 24 weeks (PASI 90 response)							
1 study[25]/478	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.8; 95% CI, 1.5 to 2.2	Moderate[e]
QoL at 24 weeks (DLQI 0 or 1)							
1 study[25]/478	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.4; 95% CI, 1.2 to 1.7	Moderate[e]
Adverse events							
1 study[25]/478	RCT	Moderate	NA	Direct	Imprecise	Dose every 4 weeks: calculated RR, 1.01; 95% CI, 0.88 to 1.2	Moderate[e]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
						Dose every 4 then 8 weeks: calculated RR, 1.03; 95% CI, 0.90 to 1.2	
Serious adverse events							
1 study[25]/478	RCT	Moderate	NA	Direct	Imprecise	Dose every 4 weeks: calculated RR, 0.81; 95% CI, 0.22 to 2.9 Dose every 4 then 8 weeks: calculcated RR, 0.20; 95% CI, 0.02 to 1.7	Low[b]
Bimekizumab (pipeline drug) vs. secukinumab							
Disease remission at 16 weeks (PASI 100 response)							
1 study[24]/743	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.3; 95% CI, 1.1 to 1.4	Moderate[e]
QoL at 48 weeks (DLQI 0 or 1)							
1 study[24]/743	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 1.02 to 1.2	Moderate[e]
Adverse events							
1 study[24]/743	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.06; 95% CI, 0.99 to 1.1	Moderate[e]
Serious adverse events							
1 study[24]/743	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.04; 95%CI, 0.58 to 1.9	Low[b]
Bimekizumab (pipeline drug) vs. ustekinumab							
Disease remission at 16 and 52 weeks (PASI 90 response)							
1 study[21]/567	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.7; 95% CI 1.5 tp 2.0 at week 16 Calculated RR, 1.5; 95% CI, 1.3 to 1.7 at week 52	Moderate[e]
QoL at 16 and 52 weeks (DLQI 0 or 1)							
1 study[21]/567	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.6; 95% CI, 1.3 to 1.9 at week 16 Calculated RR, 1.5; 95% CI, 1.3 to 1.7 at week 52	Moderate[e]
Adverse events							
1 study[21]/567	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.93 to 1.3	Moderate[e]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Serious adverse events							
1 study[21]/567	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 0.51; 95% CI, 0.15 to 1.7	Low[b]
Bimekizumab (pipeline drug) vs. placebo							
Disease remission at 12 to 20 weeks (% change in PASI or PASI 90 response)							
4 studies[21,22,38,53]/1,128	RCT	Moderate	Consistent	Direct	Precise	Significantly higher proportion achieved remission with bimekizumab vs. placebo (46% to 90% across various doses in vs. 0% to 1% for placebo)[38] Percentage change from baseline in PASI score higher for 160-mg, 480-mg, and 640-mg dosages vs. placebo[53]	High
QoL at 16 weeks (DLQI 0 or 1)							
2 studies[21,22]/839	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 13.0; 95% CI, 5.5 to 30.5 Calculated RR, 5.6; 95% CI, 3.1 to 10.0	Moderate[e]
Adverse events							
4 studies[21,22,38,53]/1,128	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.78 to 1.5 Calculated RR, 1.5; 95% CI, 1.1 to 2.0 Calculated RR, 1.7; 95% CI, 1.1 to 2.6 Calculated RR, 1.2; 95% CI, 0.94 to 1.5	Low[b]
Serious adverse events							
4 studies[21,22,38,53]/1,291	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 0.20; 95% CI, 0.01 to 3.2 Calculated RR, 0.74; 95% CI, 0.15 to 3.6 Calculated RR, 0.65; 95% CI 0.13 to 3.3 Only 1 event in the fourth study, unable to calculated RR	Low[b]
Brodalumab vs. adalimumab							
Serious infection							
1 study[28]/15,475	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.65; 95% CI, 0.18 to 2.42	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Brodalumab vs. etanercept							
Serious infection							
1 study[28] /9,841	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.79; 95% CI, 0.21 to 2.95	Very low[a]
Brodalumab vs. guselkumab							
Serious infection							
1 study[28]/706	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.58; 95% CI, 0.13 to 2.52	Very low[a]
Brodalumab vs. infliximab							
Serious infection							
1 study[28]/3,182	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.44; 95% CI, 0.12 to 1.66	Very low[a]
Brodalumab vs. ustekinumab							
Disease remission at 12 and 52 weeks (PASI 100)							
2 studies[37,81]/3,712	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieved remission (ARDs 18 and 22 percentage points at 12 weeks, 23 (studies pooled) at 52 weeks)	High
QoL at 12 and 52 weeks (DLQI 0 or 1)							
2 studies[37,82]/3,712	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieved a score of 0 or 1 (ARDs 14 at 12 weeks and 15 at 52 weeks; studies pooled)	High
Adverse events							
2 studies[37]/3,712	RCT	Moderate	Consistent	Direct	Imprecise	RRs 0.98 and 1.1, CIs of both include null effect	Moderate[e]
Serious adverse events							
2 studies[37]/3,712	RCT	Moderate	Inconsistent	Direct	Imprecise	RR, 0.74; 95% CI, 0.21 to 2.6 and RR, 2.3; 95% CI, 0.49 to 10.4	Very low[b,f]
Serious infection							
1 study[28]	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.00; 95% CI, 0.27 to 3.70	Very low[a]
Certolizumab vs. adalimumab							
Serious infection							
1 study[28]/32,146	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.94; 95% CI, 0.69 to 1.30	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Certolizumab vs. brodalumab							
Serious infection							
1 study[28]/1,201	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.45; 95% CI; 0.38 to 5.58	Very low[a]
Certolizumab pegol vs. etanercept							
Clinical improvement at 12 weeks (PASI 75)							
1 study[15]/502	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.2; 95% CI, 1.04 to 1.5 for 400-mg dose Calculated RR, 1.1; 95% CI, 0.95 to 1.4 for 200-mg dose	Moderate[e]
Adverse events							
1 study[15]/502	RCT	Moderate	NA	Direct	Imprecise	200-mg dose: calculated RR, 1.02, 95% CI, 0.81 to 1.3 400-mg dose: calculated RR, 1.06, 95% CI, 0.85 to 1.3	Moderate[e]
Serious adverse events							
1 study[15]/502	RCT	Moderate	NA	Direct	Imprecise	200-mg dose: calculated RR, 1.02, 95% CI, 0.06 to to 16.1 400-mg dose: calculated RR, 4.0, 95% CI, 0.45 to 35.6	Low[b]
Serious infection							
1 study[28]/10,691	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.15; 95% CI, 0.83 to 1.59	Very low[a]
Certolizumab pegol vs. guselkumab							
Serious infection							
1 study[28]/1,556	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.84; 95% CI, 0.41 to 1.75	Very low[a]
Certolizumab pegol vs. infliximab							
Serious infection							
1 study[28]/4,032	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.64; 95% CI, 0.46 to 0.91	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Certolizumab pegol vs. ustekinumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/31,545	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 1.09; 95% CI, 0.68 to 1.75 Adjusted HR, 1.45; 95% CI, 1.03 to 2.04	Very low[a]
Deucravacitinib (pipeline drug) vs. placebo							
Clinical improvement at 12 weeks (PASI 75)							
1 study[54]/268	RCT	Moderate	NA	Direct	Imprecise	Higher proportion achieved remission for all but lowest of 5 different doses	Moderate[e]
QoL at 12 weeks (DLQI 0 or 1)							
1 study[54]/268	RCT	Moderate	NA	Direct	Imprecise	Higher proportion with no effect of psoriasis on QoL for all but the 2 lowest of 5 different doses	Moderate[e]
Adverse events							
1 study[54]/268	RCT	Moderate	NA	Direct	Imprecise	Higher proportion at 2 highest doses (RRs 1.6 and 1.5), no difference at 3 lowest doses	Low[b]
Serious adverse events							
1 study[54]/268	RCT	Moderate	NA	Direct	Imprecise	Too imprecise for definitive conclusion, RRs for all doses very close to 1.0, but extremely wide CIs	Low[b]
Etanercept vs. adalimumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[28,59]/132,663	Cohort	Moderate	Consistent	Indirect	Imprecise	HR, 0.76; 95% CI, 0.61 to 0.94 Adjusted HR, 0.81; 95% CI, 0.72 to 0.93	Very low[a]
Major cardiovascular events							
1 study[32]/5,468	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted IRR, 0.62; 95% CI, 0.18 to 1.72	Very low[a]
Etanercept vs. infliximab							
Clinical improvement at 24 weeks (PASI 75)							
1 study[64]/50	RCT	High	NA	Direct	Imprecise	Lower proportion achieved remission (35% vs. 72%)	Very low[b,g]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
QoL at 24 weeks (relative change in SF-36 PCS and MCS)							
1 study[64]/50	RCT	High	NA	Direct	Imprecise	No difference between agents.	Very low[b,g]
Adverse events							
1 study[64]/50	RCT	High	NA	Direct	Imprecise	RR, 1.04; 95% CI, 0.93 to 1.2	Very low[b,g]
Serious adverse events							
1 study[64]/50	RCT	High	NA	Direct	Imprecise	RR, 0.36; 95% CI, 0.08 to 1.6	Very low[b,g]
Serious infection							
1 study[28]/12,663	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.56; 95% CI, 0.46 to 0.67	Very low[a]
Etanercept vs. ixekizumab							
Clinical improvement at 12 weeks (PASI 75)							
2 studies[68]/2,570	RCT	Moderate	Consistent	Direct	Precise	Lower proportion achieved remission (ARD range 31 to 48 percentage points across doses and studies)	High
Disease remission at 12 weeks (PGA 0 or 1)							
2 studies[68]/2,570	RCT	Moderate	Consistent	Direct	Precise	Lower proportion achieved remission (ARD range 34 to 47 percentage points across doses and studies)	High
QoL at 12 weeks (DLQI 0 or 1)							
2 studies[68]/2,570	RCT	Moderate	Consistent	Direct	Precise	Lower proportion achieved no or minimal effect of psoriasis on QoL (ARD 20 to 30 percentage points)	High
Adverse events							
2 studies[68]/2,570	RCT	Moderate	NA (only pooled result provided)	Direct	Imprecise	Pooled RR, 0.93; 95% CI, 0.85 to 1.02	Moderate[e]
Serious adverse events							
2 studies[68]/2,570	RCT	Moderate	NA (only pooled result provided)	Direct	Imprecise	Pooled RR, 0.99; 95% CI, 0.48 to 2.1	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Serious infection							
1 study[28]/10,429	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.22; 95% CI, 0.74 to 2.0	Very low[a]
Etanercept vs. secukinumab							
Clinical Improvement at 12 weeks (PASI 75)							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Precise	Lower proportion (44%) achieved response with etanercept vs. 300 mg secukinumab (77%) or 150 mg secukinumab (67%)	High
Disease remission at 12 weeks (PGA 0 or 1)							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Precise	Lower proportion (27%) achieved response with etanercept vs. 300 mg secukinumab (63%) or 150 mg secukinumab (51%)	High
Maintenance of disease remission at 52 weeks (continued PASI 75 response among initial responders)							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Precise	Lower proportion (73%) achieved response with vs. 300 mg secukinumab (84%) or 150 mg secukinumab (82%)	High
QoL at 12 weeks (mean change in DLQI)							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Imprecise	Lower improvement in QoL (7.9 points) for etanercept vs. 300 mg secukinumab (10.4 points) or 150 mg secukinumab (9.7 points)	Moderate[e]
Adverse events							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Imprecise	RR, 0.97; 95% CI, 0.90 to 1.1	Moderate[e]
Serious adverse events							
1 study[45]/1,306	RCT	Moderate	NA	Direct	Imprecise	RR, 1.1; 95% CI, 0.61 to 1.9	Low[b]
Serious infection							
1 study[28]/12,806	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.06; 95% CI, 0.85 to 1.35	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Etanercept vs. tildrakizumab							
Clinical improvement at 12 weeks (PASI 75)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	Lower proportion (48%) vs. 100 mg tildrakizumab (61%) or 200 mg tildrakizumab (66%)	High
Clinical improvement at 28 weeks (PASI 75)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	Lower proportion (54%) vs. 100 mg tildrakizumab (73%) or 200 mg tildrakizumab (73%)	High
QoL at 12 weeks (DLQI 0 or 1)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Lower proportion (36%) with no effect of psoriasis on QoL vs. 200 mg tildrakizumab (47%), no difference vs. 100 mg tildrakizumab (40%)	Moderate[e]
QoL at 28 weeks (DLQI 0 or 1)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	Lower proportion (39%) with no effect of psoriasis on QoL vs. 100 mg tildrakizumab (54%) or 200 mg tildrakizumab (65%)	High
Adverse events							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Reported for 2 time periods: Weeks 0 to 12: RR, 0.82; 95% CI, 0.70 to 0.96 for 100-mg dosage; RR, 0.91; 95% CI, 0.79 to 1.1 for 200-mg dosage; both vs. etanercept. Weeks 13 to 28: RR, 0.81; 95% CI, 0.69 to 0.95 for 100-mg dosage; RR, 0.80; 95% CI, 0.68 to 0.93 for 200-mg dosage.	Moderate[e]
Serious adverse events							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Reported for 2 time periods Weeks 0 to 12: RR, 0.58; 95% CI, 0.17 to 2.0 for 100-mg dosage;	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
						RR, 0.85; 95% CI, 0.29 to 2.5 for 200-mg dosage; both vs. etanercept. Weeks 13 to 28: RR, 0.63; 95% CI, 0.28 to 1.4 for 100-mg dosage; RR, 0.41; 95% CI, 0.16 to 1.1 for 200-mg dosage.	
Etanercept vs. tofacitinib (not FDA-approved for plaque psoriasis)							
Clinical improvement at 12 weeks (PASI 75)							
1 study[62,63]/1,106	RCT	Moderate	NA	Direct	Imprecise	Higher proportion (59%) achieved response vs. 5 mg tofacitinib (40%) but similar response vs. 10 mg tofacitinib (64%)	Moderate[e]
Disease remission at 12 weeks (PGA 0 or 1)							
1 study[62,63]/1,106	RCT	Moderate	NA	Direct	Imprecise	Higher proportion (66%) achieved response vs. 5 mg tofacitinib (47%) but similar response vs. 10 mg tofacitinib (68%)	Moderate[e]
QoL (Change in DLQI of 5 points or more) at 12 weeks							
1 study[62,63]/1,106	RCT	Moderate	NA	Direct	Imprecise	Higher proportion (75%) achieved response vs. 5 mg tofacitinib (66%) but similar response vs. 10 mg tofacitinib (78%)	Low[b] for 10-mg dosage Moderate[e] for 5-mg dosage
Adverse events							
1 study[62,63]/1,106	RCT	Moderate	NA	Direct	Imprecise	RR, 1.1; 95% CI, 0.92 to 1.2	Low[b]
Serious adverse events							
1 study[62,63]/1,106	RCT	Moderate	NA	Direct	Imprecise	RR, 0.98; 95% CI, 0.35 to 2.8	Low[b]
Etanercept vs. ustekinumab							
Clinical improvement (PASI 75) at 12 weeks							
1 study[51]/903	RCT	Moderate	NA	Direct	Imprecise	Lower proportion achieved remission with etanercept (57%) vs. either 45 mg	Moderate[e]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
						ustekinumab (68%) or 90 mg ustekinumab (74%).	
Adverse events							
1 study[51]/903	RCT	Moderate	NA	Direct	Imprecise	RR, 1.03; 95% CI, 0.94 to 1.1	Low[b]
Serious adverse events							
1 study[51]/903	RCT	Moderate	NA	Direct	Imprecise	RR, 0.80; 95% CI, 0.24 to 2.6	Low[b]
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/63,436	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 1.39; 95% CI, 1.01 to 1.90 Adjusted HR, 1.27; 95% CI, 1.06 to 1.49	Very low[a]
Golimumab vs. ustekinumab							
Serious infection requiring hospitalization							
1 study[27]/24,428	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.74; 95% CI, 1.00 to 3.03	Very low[a]
Guselkumab vs. adalimumab							
Disease remission at 16 weeks (PGA 0 or 1)							
3 studies[69,73,74]/1,658	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieve remission with guselkumab 100 mg vs. adalimumab (ARD range 16 to 28 percentage points)	High
QoL at 16 weeks (mean change in DLQI or DLQI 0 or 1)							
3 studies[69,73,74]/1,658	RCT	Moderate	Consistent	Direct	Imprecise	Higher proportion with no effect of psoriasis on QoL for guselkumab (ARD range 13 to 15 percentage points, but only statistically significant in 1 of the 2 studies reporting this outcome) Mean difference in change: from baseline: range −0.7 to −1.6 across the 3 studies.	Moderate[e]
Adverse Events							
3 studies[69,73,74]/1,658	RCT	Moderate	Consistent	Direct	Imprecise	RR, range from 0.89 to 1.01; all CIs include null effect.	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Serious Adverse Events							
3 studies[69,73,74]/1,658	RCT	Moderate	Consistent	Direct	Imprecise	RR, range from 0.62 to 1.4; all CIs include null effect.	Low[b]
Serious infection							
1 study[28]/15,821	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.12 (0.58 to 2.18)	Very low[a]
Guselkumab vs. etanercept							
Serious infection							
1 study[28]/10,187	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.37; 95% CI, 0.70 to 2.67	Very low[a]
Guselkumab vs. secukinumab							
Disease remission at 12 and 48 weeks (PASI 75, PASI 90)							
1 study[44,80]/1,048	RCT	Moderate	NA	Direct	Precise	Higher proportion (84%) achieved PASI 90 response vs. secukinumab (70%) at 48 weeks; proportion achieving PASI 75 response at both 12 and 48 weeks was similar (85% guselkumab vs. 80% secukinumab; $P < .001$ for noninferiority and $P = .06$ for superiority), lower proportion (69%) achieved PASI 90 response vs. secukinumab (76%) at 12 weeks but no significance testing conducted to control type I error.	Moderate[f]
Adverse events							
1 study[44,80]/1,048	RCT	Moderate	NA	Direct	Imprecise	RR, 0.95; 95% CI, 0.90 to 1.0	Low[b]
Serious adverse events							
1 study[44]/1,048	RCT	Moderate	NA	Direct	Imprecise	RR, 0.85; 95% CI, 0.54 to 1.3	Low[b]
Infliximab vs. adalimumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[28,59]/126,004	Cohort	Moderate	Consistent	Indirect	Imprecise	HR, 1.9; 95% CI, 1.01 to 3.6 Adjusted HR, 1.47; 95% CI, 1.24 to 1.74	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Infliximab vs. guselkumab							
Serious infection							
1 study[28]/3,528	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.31; 95% CI, 0.67 to 2.58	Very low[a]
Infliximab vs. ustekinumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/36,704	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 2.92; 95% CI, 1.80 to 4.72 Adjusted HR, 2.27; 95% CI, 1.85 to 2.78	Very low[a]
Ixekizumab vs. adalimumab							
Serious infection							
1 study[28]/16,063	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.67; 95% CI, 0.41 to 1.11	Very low[a]
Ixekizumab vs. brodalumab							
Serious infection							
1 study[28]/948	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.03; 95% CI, 0.26 to 4.19	Very low[a]
Ixekizumab vs. certolizumab pegol							
Serious infection							
1 study[28]/1,798	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.71; 95% CI, 0.40 to 1.28	Very low[a]
Ixekizumab vs. guselkumab							
Disease remission at 12 and 24 weeks (PASI 100)							
1 study[17,36]/1,027[28]	RCT	Moderate	NA	Direct	Precise	At 12 weeks: calculated RR, 1.7; 95% CI, 1.4 to 2.0 At 24 weeks: calculated RR, 0.96; 95% CI, 0.85 to 1.1	High
QoL at 12 and 24 weeks (DLQI 0 or 1)							
1 study[17,36]/1,027	RCT	Moderate	NA	Direct	Precise	Reported as a significant difference at 12 weeks but not at 24 weeks; only shown on figures, actual values NR	High
Adverse events at 24 weeks							
1 study[17,36]/1,027	RCT	Moderate	NA	Direct	Precise	Calculated RR, 1.1; 95% CI, 0.99 to 1.2	High

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Serious adverse events at 24 weeks							
1 study[17,36]/1,027	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.6 to 2.1	Low[b]
Serious infection							
1 study[28]/1,294	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.60; 95% CI, 0.26 to 1.37	Very low[a]
Ixekizumab vs. infliximab							
Serious infection							
1 study[28]/3,770	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.46; 95% CI, 0.27 to 0.77	Very low[a]
Ixekizumab vs. secukinumab							
Disease Remission at 24 weeks (sPGA)							
1 study[23]/54	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.01; 95% CI, 0.81 to 1.3	Moderate[e]
Clinical Improvement at 24 weeks (GPSS)							
1 study[23]/54	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.03; 95% CI, 0.73 to 1.5	Moderate[e]
Adverse events							
1 study[23]/54	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.04; 95% CI, 0.71 to 1.5	Low[b]
Serious adverse events							
1 study[23]/54	RCT	Moderate	NA	Direct	Imprecise	0 events	Very low[c]
Ixekizumab vs. ustekinumab							
Disease remission at 12 and 52 weeks (PASI 90)							
1 study[47,48,83]/302	RCT	Moderate	NA	Direct	Imprecise	Higher proportion achieved response vs. ustekinumab (73% vs. 42% at 12 weeks; 77% vs. 59% at 52 weeks)	Moderate[e]
QoL at 12 and 52 weeks (DLQI 0 or 1)							
1 study[47,48,83]/302	RCT	Moderate	NA	Direct	Imprecise	Higher proportion achieved response vs. ustekinumab (61% vs. 45% at 12 weeks; 71% vs. 57% at 52 weeks)	Moderate[e]
Adverse events							
1 study[47,48]/302	RCT	Moderate	NA	Direct	Imprecise	RR, 0.92; 95% CI, 0.80 to 1.1	Low[b]
Serious adverse events							
1 study[47,48]/302	RCT	Moderate	NA	Direct	Imprecise	RR, 0.74; 95% CI, 0.18 to 3.0	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/31,065	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 2.98; 95% CI, 1.20 to 7.41 Adjusted HR, 1.03; 95% CI, 0.62 to 1.72	Very low[a]
Risankizumab vs. adalimumab							
Disease remission at 16 weeks (PASI 90)							
1 study[46]/605	RCT	Moderate	NA	Direct	Imprecise	Higher proportion (72%) achieved response vs. adalimumab (47%)	Moderate[c]
QoL at 16 weeks (DLQI 0 or 1)							
1 study[46]/605	RCT	Moderate	NA	Direct	Imprecise	Higher proportion (66%) achieved response vs. adalimumab (49%)	Moderate[c]
Adverse events							
1 study[46]/605	RCT	Moderate	NA	Direct	Imprecise	RR, 0.98; 95% CI, 0.85 to 1.1	Low[b]
Serious adverse events							
1 study[46]/605	RCT	Moderate	NA	Direct	Imprecise	RR, 1.1; 95% CI, 0.46 to 2.7	Low[b]
Risankizumab vs. secukinumab							
Disease remission at 16 and 52 weeks (PASI 90)							
1 study[19]/327	RCT	Moderate	NA	Direct	Imprecise	ARD 8.2%; 95% CI, −2.2 to 18.6 at 16 weeks ARD 29.8%; 95% CI, 20.8 to 38.8 at 52 weeks	Moderate[e]
Adverse events							
1 study[19]/327	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.00; 95% CI, 0.87 to 1.2	Moderate[e]
Serious adverse events							
1 study[19]/327	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.5; 95% CI, 0.54 to 4.1	Low[b]
Risankizumab vs. ustekinumab							
Disease remission at 12 to 16 weeks (PASI 90)							
3 studies[52,67]/1,065	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieved response vs. ustekinumab (ARD range 28 to 37 percentage points)	High

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
QoL at 12 to 16 weeks (DLQI 0 or 1)							
3 studies[52,67]/1,065	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieved response vs. ustekinumab (ARD range 19 to 23 percentage points)	High
Adverse events							
3 studies[52,67]/1,065	RCT	Moderate	Inconsistent	Direct	Imprecise	Fewer AEs were observed for risankizumab in the later time period (weeks 17 to 52) of 1 study (RR, 0.75; 95% CI, 0.11 to 0.77). No significant differences in the other 2 studies.	Low[e,f]
Serious adverse events							
3 studies[52,67]/1,065	RCT	Moderate	Inconsistent	Direct	Imprecise	Fewer SAEs were observed in the early time period (weeks 0 to 16) of the 1 study (RR, 0.29; 95% CI, 011 to 0.77). No significant differences in the other 2 studies.	Low[e,f]
Secukinumab vs. adalimumab							
Serious infection							
1 study[28]/18,440	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.77; 95% CI, 0.62 to 0.96	Very low[a]
Secukinumab vs. brodalumab							
Serious infection							
1 study[28]/3,325	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.19; 95% CI, 0.32 to 4.48	Very low[a]
Secukinumab vs. certolizumab pegol							
Serious infection							
1 study[28]/4,175	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.82; 95% CI, 0.57 to 1.19	Very low[a]
Secukinumab vs. guselkumab							
Serious infection							
1 study[28]/3,671	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.69; 95% CI, 0.35 to 1.38	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Secukinumab vs. infliximab							
Serious infection							
1 study[28]/6,147	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.53; 95% CI, 0.41 to 0.68	Very low[a]
Secukinumab vs. ixekizumab							
Serious infection							
1 study[28]/3,913	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 1.15; 95% CI, 0.68 to 1.96	Very low[a]
Secukinumab vs. ustekinumab							
Disease remission at 16 and 52 weeks (PASI 90)							
2 studies[39-42,77]/ 1,778	RCT	Moderate	Consistent	Direct	Precise	Higher proportion achieved response vs. ustekinumab at 16 weeks (ARDs 21 and 23 percentage points) and at 52 weeks (ARDs 14 and 13 percentage points)	High
QoL at 16 and 52 weeks (DLQI 0 or 1)							
2 studies[39-42,77]/ 1,778	RCT	Moderate	NA	Direct	Precise	Higher proportion achieved response vs. ustekinumab (ARDs 15 and 13)) at 16 weeks and at 52 weeks (ARDs 12 and 8)	High
Adverse events at 16 and 52 weeks							
2 studies[39-42,77]/ 1,778[39,40]	RCT	Moderate	Consistent	Direct	Imprecise	RR range from 0.97 to 1.1 at 16 and 52 weeks, all CIs include the null effect	Moderate[e]
Serious adverse events at 16 and 52 weeks							
2 studies[39-42,77]/ 1,778[39,40]	RCT	Moderate	Consistent	Direct	Imprecise	RRs range from 1.0 to 1.6 at 16 to 52 weeks; all CIs include the null effect	Low[b]
Serious infection (requiring hospitalization in 1 study)							
2 studies[27,28]/38,333	Cohort	Moderate	Consistent	Indirect	Imprecise	Adjusted HR, 1.84; 95% CI, 1.24 to 2.72 Adjusted HR, 1.19; 95% CI, 0.93 to 1.52	Very low[a]
Antibiotics for respiratory or urinary tract infection							
1 study[31]/1,955	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted IRR, 1.22; 95% CI, 1.03 to 1.43	Very low[a]
Severe respiratory or urinary tract infection							
1 study[31]/1,955	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted IRR, 0.96; 95% CI, 0.57 to 1.61	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Candidiasis							
1 study[31]/1,955	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted IRR, 1.80; 95% CI, 0.84 to 3.84	Very low[a]
Tildrakizumab vs. etanercept							
Clinical improvement at 12 weeks (PASI 75)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	Higher proportion for 100-mg tildrakizumab (61%) and 200-mg tildrakizumab (66%) vs. etanercept (48%)	High
Clinical improvement at 28 weeks (PASI 75)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	Higher proportion for 100-mg tildrakizumab (73%) and 200-mg tildrakizumab (73%) vs. etanercept (54%)	High
QoL at 12 weeks (DLQI 0 or 1)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Higher proportion for 200-mg tildrakizumab (47%) vs. etanercept (36%); but no difference vs. 100-mg tildrakizumab (40%)	Moderate[e]
QoL at 28 weeks (DLQI 0 or 1)							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Precise	High proportion for 100-mg tildrakizumab (54%) and 200-mg tildrakizumab (65%) vs. etanercept (39%)	High
Adverse events							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Reported for 2 time periods: Weeks 0 to 12: RR, 0.82; 95% CI, 0.70 to 0.96 for 100-mg dosage; RR, 0.91; 95% CI, 0.79 to 1.1 for 200-mg dosage; both vs. etanercept. Weeks 13 to 28: RR, 0.81; 95% CI, 0.69 to 0.95 for 100-mg dosage; RR, 0.80; 95% CI, 0.68 to 0.93 for 200-mg dosage	Moderate[e]
Serious adverse events							
1 study[65]/1,090	RCT	Moderate	NA	Direct	Imprecise	Reported for 2 time periods Weeks 0 to 12: RR, 0.58; 95% CI, 0.17 to 2.0 for 100-mg dosage;	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
						RR, 0.85; 95% CI, 0.29 to 2.5 for 200-mg dosage; both vs. etanercept. Weeks 13 to 28: RR, 0.63; 95% CI, 0.28 to 1.4 for 100-mg dosage; RR, 0.41; 95% CI, 0.16 to 1.1 for 200-mg dosage.	
Ustekinumab vs. adalimumab							
Serious infection (requiring hospitalization in 1 study)							
2 studies[28,59]/129,660	Cohort	Moderate	NA	Indirect	Imprecise	HR, 0.70; 95% CI, 0.49 to 1.0 Adjusted HR, 0.65; 95% CI, 0.56 to 0.76	Very low[a]
Major cardiovascular events							
1 study[32]/5,468	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted IRR, 1.30; 95% CI, 0.46 to 3.24	Very low[a]
Ustekinumab vs. guselkumab							
Serious infection							
1 study[28]/7,184	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 0.58; 95% CI, 0.30 to 1.14	Very low[a]
Ustekinumab vs. TNF-α inhibitors							
Incident atrial fibrillation							
1 study[58]/60,028	Cohort	Moderate	NA	Indirect	Imprecise	Incident atrial fibrillation: Adjusted HR, 1.08; 95% CI, 0.76 to 1.54	Very low[a]
Major cardiovascular events							
2 studies[32,58]/65,496	Cohort	Moderate	Consistent	Indirect	Imprecise	Major cardiovascular events Adjusted HR, 1.10; 95% CI, 0.80 to 1.52 Adjusted IRR, 1.47; 95% CI, 0.53 to 3.52	Very low[a]
Various biologics (etanercept, infliximab, ustekinumab, others) vs. adalimumab							
Various adverse events							
1 study[57]/10,065	Cohort	Moderate	NA	Indirect	Imprecise	Adjusted HR, 95% CI Abnormal lab results: 0.96; 0.85 to 1.09 Infection: 1.02; 0.96 to 1.08 Mental disorder: 1.03; 0.93 to 1.13 Cardiovascular disease: 1.14; 0.95 to 1.35 Malignancy: 0.87; 0.67 to 1.13 Respiratory disease: 1.23; 0.99 to 1.54	Very low[a]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Certainty of Evidence
Anti-IL 17 agents vs. anti-IL 12/23 agents vs. anti-TNF-α agents							
Serious infection							
1 study[30]/9,305	Cohort	Moderate	NA	Indirect	Imprecise	Anti-IL 17 vs. anti-TNF-α: HR, 0.89; 95% CI, 0.48 to 1.66 Anti-IL 12/23 vs. anti-TNF-α: IRR, 0.59; 95% CI, 0.39 to 0.90	Very low[d]
Hepatic AEs							
1 study[29]/4,280 person-years	Cohort	High	NA	Direct	Imprecise	Anti-IL 17 vs. anti-TNF-α: IRR, 1.46; 95% CI, 0.75 to 2.85 Anti-IL 12/23 vs. anti-TNF-α: IRR, 1.15; 95% CI, 0.64 to 2.08	Very low[d,g]

Notes: [a] Started at low and downgraded for indirectness and imprecision. [b] Downgraded 2 levels for imprecision. [c] Downgraded 3 levels for very serious imprecision. [d] Started at low for study design and downgraded for imprecision. [e] Downgraded 1 level for imprecision. [f] Downgraded 1 level for inconsistency across time points . [g] Downgraded 1 level for study limitations.

Abbreviations: AE: adverse event; ARD: absolute risk difference; CI: confidence interval; DLQI: Dermatology Life Quality Index; FDA: US Food and Drug Administration; GPSS: Genital Psoriasis Symptom Scale; HR: hazard ratio; IL: interleukin; IRR: incidence rate ratio; mg: milligram; NA: not applicable; NR: not reported; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); PGA: Physician's Global Assessment; QoL: QoL; RCT: randomized controlled trial; RoB: risk of bias; RR: risk ratio; SAE: serious adverse event; SD: standard deviation; SF-36: short form 36 survey; SF-36 MCS: Short Form Survey Mental Health Component Score; SF-36 PCS: Short Form Survey Physical Health Component Score; sPGA: Static Physicians Global Assessment; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha; vs.: versus.

Table C2. Evidence Profile of Comparisons of TIMs for Treatment of Psoriatic Arthritis

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Overall Quality of the Evidence
Adalimumab vs. etanercept and infliximab							
Clinical improvement at 1 year (ACR20)							
1 study[50]/100	RCT	High	NA	Direct	Imprecise	70% vs. 72% vs. 75% (*P* NR)	Very low[a,b]
Adverse events							
1 study[50]/100	RCT	High	NA	Direct	Imprecise	Calculated RR, 0.38; 95% CI, 0.17 to 0.84 for adalimumab vs. etanercept Calculated RR, 0.23; 95% CI, 0.11 to 0.49 for adalimumab vs. infliximab Calculated RR, 1.6; 95% CI, 1.1 to 2.4 for infliximab vs. etanercept	Very low[a,b]
Incidence of tuberculosis							
1 study[56]/10,434	Cohort	High	NA	Unclear	Imprecise	Compared with infliximab (1.27%); 0.57% (adalimumab, *P* = .008) 0.30% (etanercept, *P* < .001) Adalimumab vs. etanercept, *P* = .08	Very low[a,b]
Adalimumab vs. tofacitinib							
Clinical improvement at 12 months (ACR20)							
1 study[60,61]/422	RCT	Moderate	NA	Direct	Imprecise	60% vs. 70% (tofacitinib 10 mg) vs. 68% (tofacitinib 5 mg) (*P* NR)	Low[b]
Skin disease remission at 12 months (PASI 75)							
1 study[60,61]/422	RCT	Moderate	NA	Direct	Imprecise	56% vs. 67% (tofacitinib 10 mg) vs. 56% (tofacitinib 5 mg) (*P* NR)	Low[b]
QoL at 3 months (mean change in SF-36 PCS from baseline)							
1 study[60,61]/422	RCT	Moderate	NA	Direct	Imprecise	6.2 points vs. 5.7 (tofacitinib 10 mg) vs. 5.5 (tofacitinib 5 mg) (*P* NR)	Low[b]
Adverse events							
1 study[60,61]/422	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.90 to 1.3	Low[b]
Serious adverse events							
1 study[60,61]/422	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.46 to 2.8	Very low[c]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Overall Quality of the Evidence
Bimekizumab (pipeline drug) vs. placebo							
Clinical improvement at 12 weeks (ACR 50)							
1 study[20]/83	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 3.7; 95% CI, 1.01 to 13.7	Low[b]
QoL at 12 weeks (mean change in HAQ-DI)							
1 study[20]/83	RCT	Moderate	NA	Direct	Imprecise	Calculated mean difference, −0.3; 95% CI, −0.52 to −0.08	Low[b]
Adverse events							
1 study[20]/83	RCT	Moderate	NA	Direct	Imprecise	Calculated RR 0.85; 0.57 to 1.3	Very low[c]
Serious adverse events							
1 study[20]/83	RCT	Moderate	NA	Direct	Imprecise	1 event in placebo group, 0 events in active treatment group	Very low[c]
Ixekizumab vs. adalimumab							
Clinical improvement at 24 weeks (ACR 20)							
2 studies[18,33,34,66]/983	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 0.96; 95% CI, 0.86 to 1.1 in 1 study; 57% vs. 62% (ixekizumab every 2 weeks) vs. 58% (ixekizumab every 4 weeks) in other study (*P* NR)	Moderate[d]
Clinical improvement at 24 weeks (PASI 75)							
2 studies[18,33,34,66]/983	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 1.2; 95% CI, 1.06 to 1.3) in 1 study; 54% vs. 80% (ixekizumab every 2 weeks) vs. 71% (ixekizumab every 4 weeks) (*P* NR) in other study	Moderate[d]
Adverse events							
2 studies[18,33,34,66]/983	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.97 to 1.2) Calculated RR, 1.0; 95% CI, 0.83 to 1.3	Low[b]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Overall Quality of the Evidence
Serious adverse events							
2 studies[18,33,34,66]/983	RCT	Moderate	Consistent	Direct	Imprecise	Calculated RR, 0.34; 95% CI, 0.18 to 0.65 Calculated RR 0.59; 95% CI, 0.15 to 2.4	Very low[c]
Secukinumab vs. adalimumab							
Clinical improvement at 52 weeks (ACR20)							
1 study[16,35]/853	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.1; 95% CI, 0.98 to 1.2	Moderate[d]
Clinical improvement at 52 weeks (PASI 90)							
1 study[16,35]/853	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.5; 95% CI, 1.3 to 1.7	Moderate[d]
QoL at 52 weeks (change in HAQ-DI)							
1 study[16,35]/853	RCT	Moderate	NA	Direct	Imprecise	Difference in mean change, −0.02 (−0.10 to 0.05)	Moderate[d]
Adverse events							
1 study[16,35]/853	RCT	Moderate	NA	Direct	Imprecise	Calculated RR 0.98; 95% CI, 0.91 to 1.1	Moderate[d]
Serious adverse events							
1 study[16,35]/853	RCT	Moderate	NA	Direct	Imprecise	Calculated RR 1.1; 95% CI, 0.70 to 1.9	Low[b]
Upadacitinib vs. adalimumab							
Clinical improvement at 12 weeks (ACR20)							
1 study[26]/1,281	RCT	Moderate	NA	Direct	Imprecise	15-mg dose, calculated RR 1.1; 95% CI, 0.99 to 1.2 30-mg dose, calculated RR 1.2; 95% CI, 1.1 to 1.3	Moderate[d]
QoL at 12 weeks (change in HAQ-DI)							
1 study[26]/1,281	RCT	Moderate	NA	Direct	Imprecise	30-mg dose Difference in mean change: −0.14; 95% CI, −0.20 to −0.07	Moderate[d]

Number of Studies/Participants	Design	RoB	Consistency	Directness	Precision	Magnitude of Effect	Overall Quality of the Evidence
Adverse events							
1 study[26]/1,281	RCT	Moderate	NA	Direct	Imprecise	Calculated RR 1.1; 95% CI, 1.02 to 1.2) for 30 mg dose	Moderate[d]
Serious adverse events							
1 study[26]/1,281	RCT	Moderate	NA	Direct	Imprecise	Calculated RR, 1.6; 95% CI, 0.9 to 3.0 for 30 mg dose	Low[b]
Ustekinumab vs. TNF-α inhibitors[e]							
Enthesitis remission at 24 weeks (SPARCC EI 0)							
1 study[43]/47	RCT	High	NA	Direct	Imprecise	Higher proportion achieved response (74%) vs. TNF-α inhibitors (42%)	Very low[a,b]
Arthritis remission at 24 weeks (tender and swollen joint count of 0)							
1 study[43]/47	RCT	High	NA	Direct	Imprecise	Tender joint count (54% vs. 46%, *P* = .78) Swollen joint count (59% vs. 46%, *P* = .38)	Very low[a,b]
Skin disease remission at 24 weeks (PASI 90)							
1 study[43]/47	RCT	High	NA	Direct	Imprecise	Higher proportion achieved response (86%) vs. TNF-α inhibitors (29%)	Very low[a,b]
QoL over 24 weeks (SF-36 PCS and MCS)							
1 study[43]/47	RCT	High	NA	Direct	Imprecise	Statistically significantly larger improvements in SF-36 PCS vs. TNF-α inhibitors; no difference in SF-36 MCS vs. TNF-α inhibitors	Very low[a,b]

Notes: [a] Downgraded 1 level for study limitations. [b] Downgraded 2 levels for imprecision. [c] Downgraded 3 levels for very serious imprecision. [d] Downgraded 1 level for imprecision. [e] Enrolled only participants with active enthesitis.

Abbreviations. ACR: American College of Rheumatology percentage improvement; CI: confidence interval; HAQ-DI: Health Assessment Questionnaire–Disability Index; mg: milligram; NA: not applicable; NR: not reported; PASI: Psoriasis Area and Severity Index (number indicates percent improvement); RCT: randomized controlled trial; RR: risk ratio; SF-36 MCS: short form 36 survey mental health component score; SF-36 PCS: short form survey 36 physical health component score; SPARCC EI: Spondyloarthritis Research Consortium of Canada Enthesitis Index; TIM: targeted immune modulator; TNF-α: tumor necrosis factor alpha; vs.: versus.

Appendix D. Instruments Used to Measure Outcomes in Trials of TIMs

Table D1. Instruments Used to Measure Outcomes in Trials of TIMs for Plaque Psoriasis and Psoriatic Arthritis

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
ACR 20/50/70	American College of Rheumatology; numbers refer to percentage improvement	PsA	Improvement is defined by at least 20%/50%/70% improvement in TJC and in SJC, and at least 20%/50%/70% improvement in 3 of the 5 measures: ESR or CRP, PGA of disease activity, PtGA of disease activity, patient assessment of pain (VAS), and disability (HAQ).	Larger % improvement is better
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index	PsA	Based on response to 6 questions assessing 5 major symptoms including fatigue, spinal pain, arthralgia, enthesitis, morning stiffness duration, and morning stiffness severity.	0 to 10, higher is worse
BASFI	Bath Ankylosing Spondylitis Function Index	PsA	Based on 8 performance-based tests including climbing stairs, bending, reaching up, putting on socks, reclining and declining from a chair, getting up from the floor, looking over the shoulder, and a physically demanding activity.	0 to 10, higher is worse
BSA	Body Surface Area	PP	Percentage of total body surface area affected by psoriasis, where handprint equates to about 1% body surface area.	0 to 100, higher is worse
DAPSA	Disease Activity Index for Psoriatic Arthritis	PsA	Composite measure of disease activity that uses TJC, SJC, PtGA (scale of 0 to 10) and pain (scale of 0 to 10).	0 to 4, remission; 5 to 14, low; 15 to 28, moderate; > 28, high
DAS	Disease Activity Score	PsA	Combined index from swollen joints, tender joints, acute-phase response and patient self-report of general health that measures disease activity.	0 to 10, higher is worse
DAS-CRP	Disease Activity Score with C-reactive protein	PsA	Measure of disease activity based on TJC, SJC, PtGA of disease, and C-reactive protein levels.	0 to 100, higher is worse
DLQI	Dermatology Life Quality Index	PP	10-item questionnaire covering 6 dimensions (symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment) that assesses the overall impact of skin disorders and current treatments on the patient's functioning and well-being.	0 to 30, higher is worse

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
EQ-5D	EuroQoL 5 Dimensions	PP, PsA	Descriptive system of health-related QoL states consisting of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each of which can take 1 of 3 responses. The responses record 3 levels of severity (no problems/some or moderate problems/extreme problems) within a particular EQ-5D dimension.	0 to 1, higher is better
EQ-VAS	EuroQoL–Visual Analog Scale	PP, PsA	Patient-reported description of health status measured on a vertical visual analog scale.	0 to 100, higher is better
FACIT-F	Functional Assessment of Chronic Illness Therapy–Fatigue	PP, PsA	Thirteen items to measure fatigue during usual daily activities over the past week.	0 to 52, higher is better
GPSS	Genital Psoriasis Symptom Scale	PP	Patient-reported 8-item symptom scale assessing the severity of symptoms of genital psoriasis lesions (itch, pain, discomfort, stinging, burning, redness, scaling, and cracking); each symptom rated 0 (no symptom) to 10 (worse imaginable) and items scores are summed for total score.	0 to 80, higher is worse
HADS	Hospital Anxiety and Depression Scale	PP, PsA	Self-administered measure used to screen for the presence of depression and anxiety.	0 to 21, higher is worse
HAQ	Health Assessment Questionnaire	PP, PsA	Five generic patient-centered health dimensions: (1) to avoid disability; (2) to be free of pain and discomfort; (3) to avoid adverse treatment effects; (4) to keep dollar costs of treatment low; and (5) to postpone death.	Depends on which version used; full HAQ vs. 2-page version
HAQ-DI	Health Assessment Questionnaire - Disability Index	PP, PsA	Patient's level of functional ability; includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. There are 20 questions in 8 categories of functioning, which represent a comprehensive set of functional activities—dressing, rising, eating, walking, hygiene, reach, grip, and usual activities. Each item is scored from 0 (no difficulty) to 3 (unable to do).	0 to 60, higher is worse
HAQ-S	Health Assessment Questionnaire for the Spondylo-arthropaties	PsA	Five generic patient-centered health dimensions: (1) to avoid disability, (2) to be free of pain and discomfort, (3) to avoid adverse treatment effects, (4) to keep dollar costs of treatment low, and (5) to postpone death and 6 additional items specific for spondyloarthropathies.	0 to 60, higher is worse

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
ISI	Itch Severity Index	PP	Assess severity of itching due to psoriasis.	0 to 10, higher is worse
LDI-B	Leeds Dactylitis Index–Basic	PsA	Evaluation of finger size and pain to assess for the presence of dactylitis.	1 or 0, presence or absence of tenderness
LEI	Leeds Enthesitis Index	PsA	Measures pain and tenderness at lateral elbow epicondyle, medial femoral condyle, and Achilles tendon insertion; measures are bilateral.	0 to 6, higher is worse
MASES	Maastrict Ankylosing Spondylitis Enthesitis Score	PsA	Based on clinical examination by assessor of 13 sites.	0 to 13, higher is worse
mCPDAI	Modified Composite Psoriatic Disease Activity Index	PsA	Disease involvement is assessed in up to 5 domains: peripheral joints, skin, entheseal, dactylitis, and spinal manifestations. For each domain, individual instruments are used to assess the extent of disease activity as well as the impact on patient function and health-related QoL.	0 to 15, higher is worse
MGH-SFQ	Massachusetts General Hospital-Sexual Functioning Questionnaire	PP, PsA	Self-administered questionnaire designed to detect sexual dysfunction in 5 domains: sexual interest, excitation, orgasm, erection (only in males), and global sexual satisfaction.	0 to 20, higher is better
mSHARP	Modified Sharp Score	PsA	Assesses radiographic progression based on erosions and joint space evaluation (as is done for rheumatoid arthritis) and additional evaluated shaft periostitis, juxta-articular periostitis, and tuft resorption. Scoring is done across multiple joints in the hands and feet.	0 to 270 erosion, 0 to 160 joint space, additional ranges for the other elements
mTSS	Modified Total Sharp Score	PsA	Standard scoring method for analyzing radiographs to assess disease progression.	0 to 10, higher is worse
NAPSI	Nail Psoriasis and Severity Index	PP	The nail plate, including nail pitting, leukonychia, red spots in the lunula, and crumbling in each quadrant of the nail. Nail bed psoriasis, including onycholysis, oil drop (salmon patch) dyschromia, splinter hemorrhages, and nail bed hyperkeratosis in each quadrant of the nail. 0 if the findings are not present, 1 if they are present in 1 quadrant of the nail, 2 if present in 2 quadrants of a nail, 3 if present in 3 quadrants of a nail, and 4 if present in 4 quadrants of a nail. Thus, each nail has a matrix score	0 to 8, higher is worse

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
			(0 to 4) and a nail bed score (0 to 4), and the total nail score is the sum of those 2 (0 to 8).	
NRS	Numeric Rating Scale	PP, PsA	Unidimensional measure of pain intensity. It is a segmented numeric version of the VAS in which a respondent selects a whole number (0 to 10 integers) that best reflects the intensity of their pain.	0 to 10, higher is worse
PAI	Patient's Assessment of Itching	PP	Itch questionnaire designed to evaluate the severity of pruritus.	0 to 5, higher is worse
PASDAS	Psoriatic Arthritis Disease Activity Score	PsA	Patient and physician global scores of skin and joint disease, in addition to assessment of dactylitis, enthesitis, physical function, QoL, acute-phase response.	0 to 10, higher is worse
PASI	Psoriasis Area and Severity Index	PP	Based on the extent of the skin-surface area involved and the severity of erythema, desquamation, and plaque induration. Response to treatment can be reported by change in absolute PASI score, or more commonly by proportion of participants achieving a 50% reduction in score (PASI 50), 75% reduction in score (PASI 75), 90% reduction in score (PASI 90) or 100% reduction in score (PASI 100).	0 to 72, higher is worse
PGA/IGA	Physician or Investigator Global Assessment	PP	A 5-point or 6-point assessment assigned by physician or investigator based on the extent of skin involvement.	0 to 5 (or 6), with 0 representing clear skin, and 5 (or 6) representing severe and extensive involvement
PGPA	Patient's Global Psoriasis Assessment	PP	Single self-explanatory item to be completed by the patient, evaluating overall cutaneous disease at a specific point in time.	0 to 10, higher is worse
PsAID	Psoriatic Arthritis Impact of Disease	PsA	Patient-derived and patient-reported outcome measure for assessing the impact of psoriatic arthritis on participants' lives.	0 to 10, higher is worse
PsARC	Psoriatic Arthritis Response Criteria	PsA	Response is defined by improvement in at least 2 of the 4 following measures, 1 of which must be joint swelling or tenderness, and no worsening in any of the 4 measures: PtGA of articular disease (1–5) and PGA of articular disease (1–5), improvement being a decrease by 1 category, worsening being an increase by 1 category; joint pain/tenderness score and joint	0 to 100, higher is better

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
			swelling score, improvement being a decrease by 30%, worsening being an increase by 30%.	
P-SIM	Psoriasis Symptoms and Impacts Measure	PP	A 14-item patient-reported measure that assesses the severity of key signs, symptoms, and effects of psoriasis collected daily using a 0 (none) to 10 (very severe) NRS.	No summary score produced
PSS	Psoriasis Symptom Scale	PP	Uses 4 items to measure the severity of pain, itching, redness, and burning during the previous 24 hours.	0 to 5, higher is worse
PSSD	Psoriasis Symptoms and Signs Diary	PP	Measures 6 symptoms (itch, skin tightness, burning, stinging, and pain) and 6 signs (dryness, cracking, scaling, shedding/flaking, redness, and bleeding).	0 to 100, higher is worse
PtGA	Patient Global Assessment	PP, PsA	A 5- or 6-point assessment assigned by patient based on the extent of skin involvement.	0 to 5, with 0 representing clear skin, and 5 representing severe and extensive involvement
SF–36	Short Form 36-item Health Survey	PP, PsA	Measures the general level of well-being, consists of 8 domains reflecting 8 dimensions of life: PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; and MH, mental health. PCS is a subscale for physical health dimensions and MCS is a subscale for mental health dimensions.	0 to 100, higher is better
sIGA	Static Investigator Global Assessment	PP	Global score of vitiligo severity for the entire body. It incorporates location, distribution, size, depigmentation within lesions, and presence or absence of signs of activity.	0 to 5, higher is worse
SPARCC EI	Spondyloarthritis Research Consortium of Canada Enthesitis Index	PsA	Based on clinical assessment by evaluator on 9 bilateral sites, but inferior patella and tibial tuberosity are considered 1 site for scoring purposes.	0 to 16, higher is worse
sPGA	Static Physician's Global Assessment	PP	Physician's global assessment of the subject's psoriasis based on severity of induration, scaling, and erythema.	0 to 5, higher is worse
VAS	Visual Analog Scale	PP, PsA	Psychometric response scales used to measure subjective acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between "no pain" and "worst pain."	0 to 10, higher is worse

Abbreviation	Name	Condition(s) Used in	General Description	Range and Direction
WLQ	Work Limitations Questionnaire	PP, PsA	Twenty-five items that aggregate into 4 scales : time management, physical demands, mental-interpersonal demands, and output demands.	0 to 100, higher is worse
WPAI-PSO	Work Productivity and Activity Impairment - Psoriasis	PP	Assesses 4 dimensions: absenteeism, presenteeism, work productivity loss, and activity impairment; scores expressed as percentages.	0 to 100%, higher is worse

Abbreviations. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PP: plaque psoriasis; PsA: psoriatic arthritis; QoL: quality of life; SJC: swollen joint count; TIM: targeted immune modulator; TJC: tender joint count; vs.: versus.

Appendix E. Bibliography of Included Studies

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Appendix F. Bibliography of Excluded Studies

Exclusion Code X1: Ineligible comparator (30 studies)

- Blauvelt A, Lebwohl MG, Mabuchi T, et al. Long-term efficacy and safety of ixekizumab: a 5-year analysis of the UNCOVER-3 randomized controlled trial. *J Am Acad Dermatol.* 2021;85(2):360-368. doi: 10.1016/j.jaad.2020.11.022. Exclude: X1
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psoriasis and psoriatic arthritis. *Clin Epidemiol.* 2020;12:153-161. doi: 10.2147/CLEP.S239511. Exclude: X1

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Exclusion Code X2: Ineligible Study Design (29 studies)

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Exclusion Code X3: Ineligible Outcome (11 studies)

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- Wright S, Alloo A, Strunk A, Garg A. Real-world risk of new-onset inflammatory bowel disease among patients with psoriasis exposed to interleukin 17 inhibitors. *J Am Acad Dermatol.* 2020;83(2):382-387. doi: 10.1016/j.jaad.2020.04.010. Exclude: X3
- Yiu ZZN, Mason KJ, Hampton PJ, et al. Drug survival of adalimumab, ustekinumab and secukinumab in patients with psoriasis: a prospective cohort study from the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). *Br J Dermatol.* 2020;183(2):294-302. doi: 10.1111/bjd.18981. Exclude: X3

Exclusion Code X4: Ineligible Population (3 studies)

- Merola JF, Papp KA, Nash P, et al. Tofacitinib in psoriatic arthritis patients: skin signs and symptoms and health-related quality of life from two randomized phase 3 studies. *J Eur Acad Dermatol Venereol.* 2020;34(12):2809-2820. doi: 10.1111/jdv.16433. Exclude: X4
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Exclusion Code X5: Ineligible Intervention (2 studies)

- Atalay S, van den Reek J, den Broeder AA, et al. Comparison of tightly controlled dose reduction of biologics with usual care for patients with psoriasis: a randomized clinical trial. *JAMA Dermatol.* 2020;156(4):393-400. doi: 10.1001/jamadermatol.2019.4897. Exclude: X5
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Exclusion Code X6: Ineligible Country (1 study)

- Zhu SM, Wang WH, Guo JZ, et al. Effectiveness and safety of secukinumab in Chinese patients with plaque psoriasis in a clinical practice setting: a pilot study. *Chin Med J (Engl).* 2020;133(24):3017-3019. doi: 10.1097/cm9.0000000000001258. Exclude: X6

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