

Comparative Efficacy and Safety of Biologic Therapies for Moderate-to-Severe Psoriasis: A Systematic Review of Randomized Controlled Trials

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Abstract

Psoriasis is a chronic, immune-mediated dermatological condition marked by cycles of remission and relapse. Among its subtypes, plaque psoriasis is the most prevalent, accounting for approximately 90% of cases. In patients with moderate-to-severe disease, systemic therapy is often warranted. Biologic therapies, developed over the past two decades, have revolutionized the therapeutic landscape by targeting specific immunological pathways such as TNF- α , IL-12/23, IL-17, and IL-23. While numerous biologics have demonstrated individual efficacy and safety in randomized controlled trials (RCTs), direct comparisons remain limited, creating challenges in clinical decision-making. To conduct a systematic review of randomized controlled trials to evaluate and compare the clinical efficacy and safety profiles of currently approved biologic therapies for moderate-to-severe plaque psoriasis, thereby guiding evidence-based therapeutic choices. This systematic review followed PRISMA 2020 guidelines. A thorough search was performed in PubMed, Embase, Cochrane CENTRAL, and ClinicalTrials.gov for RCTs published from January 2010 to March 2025. Inclusion criteria were RCTs involving adults with moderate-to-severe plaque psoriasis treated with FDA- or EMA-approved biologic agents. Data were extracted on PASI 75, PASI 90, and PASI 100 response rates at 12–16 weeks, along with rates of adverse events (AEs), serious adverse events (SAEs), and discontinuation. A total of 28 studies were included in the qualitative synthesis. IL-17 inhibitors (secukinumab, ixekizumab, brodalumab) and IL-23 inhibitors (guselkumab, risankizumab, tildrakizumab) consistently achieved higher rates of complete or near-complete skin clearance (PASI 90/100) compared to TNF- α inhibitors and ustekinumab. TNF- α inhibitors, while effective, demonstrated comparatively lower response rates and a modestly higher frequency of treatment-related AEs. Ustekinumab maintained a favorable safety profile but lower efficacy relative to newer biologics. Rates of serious adverse events remained low and comparable across most agents. Newer generation biologics targeting IL-17 and IL-23 pathways demonstrate superior efficacy in achieving rapid and sustained skin clearance in moderate-to-severe psoriasis. Safety profiles were generally favorable, though slight variations in AE profiles necessitate individualized patient assessments. These findings underscore the need for personalized treatment algorithms based on disease severity, comorbidities, and patient preferences.

Keywords: Biologic therapies; Moderate-to-severe psoriasis; Plaque psoriasis; PASI 90; IL-17 inhibitors; IL-23 inhibitors; TNF-alpha inhibitors; Comparative efficacy; Safety profile;

1. Introduction

1.1 Background

Psoriasis is a chronic, immune-mediated inflammatory disorder characterized by abnormal keratinocyte proliferation and differentiation, resulting in erythematous, scaly plaques most commonly affecting the elbows, knees, scalp, and lower back. It is a multisystem disease with strong genetic, environmental, and immunological underpinnings. Affecting approximately 2–3% of the global population, psoriasis is more than just a dermatologic condition—it is increasingly recognized as a systemic disease associated with multiple comorbidities, including psoriatic arthritis, cardiovascular disease, metabolic syndrome, obesity, and depression.

Among the various clinical types of psoriasis, plaque psoriasis is the most prevalent, accounting for nearly 90% of all cases. Patients with moderate-to-severe disease, often defined as a Psoriasis Area and Severity Index (PASI) ≥ 10 , Body Surface Area (BSA) $\geq 10\%$, or Dermatology Life Quality Index (DLQI) > 10 , usually require systemic therapy. While conventional agents like methotrexate, cyclosporine, and acitretin have long been used, their side effect profiles and limited long-term efficacy have led to a shift toward biologic therapies.

Biologic agents represent a targeted approach to psoriasis treatment, focusing on key cytokines within the IL-23/Th17 axis, the primary immunological pathway implicated in disease pathogenesis. These agents are classified into four major categories based on their molecular targets:

- **TNF- α inhibitors:** adalimumab, etanercept, infliximab
- **IL-12/23 inhibitor:** ustekinumab
- **IL-17 inhibitors:** secukinumab, ixekizumab, brodalumab
- **IL-23 inhibitors:** guselkumab, risankizumab, tildrakizumab

These therapies have significantly improved clinical outcomes, offering **rapid skin clearance**, **sustained remission**, and **enhanced quality of life**. However, their varying efficacy, immunogenicity, dosing schedules, costs, and side effect profiles have created complexity in choosing the most appropriate biologic for each patient.

1.2 Rationale

Although biologic agents have become the cornerstone of systemic therapy for moderate-to-severe psoriasis, **head-to-head comparisons** are limited, and most available evidence comes from **placebo-controlled RCTs**. While indirect comparisons through **network meta-analyses** and **observational registries** have attempted to address this gap, their conclusions are often confounded by differences in trial design, patient populations, endpoints, and statistical models.

Furthermore, each biologic has unique characteristics. For instance:

- **TNF- α inhibitors**, while widely used and relatively cost-effective, are often associated with **lower PASI 90/100 response rates** and carry a slightly higher risk of **serious infections**.
- **IL-17 inhibitors** demonstrate rapid onset and high efficacy but have been linked with **candida infections** and **IBD exacerbations**.
- **IL-23 inhibitors** offer promising durability and safety, with **less frequent dosing schedules**, making them an attractive long-term option.

In this context, there remains a critical need for systematic, up-to-date comparative evaluations using cons-

istent endpoints such as PASI response rates and adverse event profiles to inform clinical decision-making.

1.3 Objective

The primary aim of this systematic review is to compare the efficacy and safety of all currently approved biologic therapies for the treatment of moderate-to-severe plaque psoriasis. Specifically, this review seeks to:

- Quantify and contrast **PASI 75, PASI 90, and PASI 100 response rates** across different biologic agents.
- Assess the **incidence of adverse events (AEs), serious adverse events (SAEs), and treatment discontinuation rates**.
- Evaluate **subgroup trends**, where data are available, such as **patients with psoriatic arthritis, treatment-naïve vs. experienced**, or those with specific comorbidities.

By synthesizing high-level evidence from randomized controlled trials, this study aims to provide clinicians with an evidence-based guide for **personalized treatment selection**.

1.4 Significance

This review is timely and clinically relevant, especially in the context of rising biologic utilization and an increasing emphasis on precision medicine. The treatment landscape for psoriasis is expanding rapidly, but the absence of clear comparative guidance poses challenges for dermatologists, rheumatologists, and other prescribing clinicians.

Understanding the relative advantages and limitations of each biologic—both in terms of clinical response and safety risks—is essential for:

- **Shared decision-making** with patients
- Managing expectations regarding **speed and durability of response**
- Considering **long-term safety**, especially in **young patients** or those with **immune-compromising conditions**
- Addressing **payer concerns** related to cost-effectiveness and formulary placement

Ultimately, this review intends to bridge the knowledge gap by delivering a comprehensive, side-by-side comparison of biologic options based on the most robust evidence available. This may support the development of future treatment algorithms, guidelines, and policy frameworks that promote better health outcomes for individuals with moderate-to-severe psoriasis.

2. Methods

2.1 Search Strategy & Study Selection

A **comprehensive literature search** was performed using four major electronic databases:

- **PubMed/MEDLINE**
- **Embase**
- **Cochrane Central Register of Controlled Trials (CENTRAL)**
- **ClinicalTrials.gov**

The search was conducted for publications from **January 1, 2010, to March 31, 2025**. This period was selected to include contemporary biologic therapies and exclude outdated or withdrawn treatments.

The search strategy combined **MeSH terms** and **free-text keywords**, incorporating both generic and brand names of biologic therapies, along with psoriasis-related terms and outcome measures. Boolean operators (AND/OR) and truncation were used to optimize sensitivity.

Additionally, we conducted **hand searches** of the references cited in relevant reviews, meta-analyses, and included trials to identify studies not captured in the electronic search.

The study selection process was conducted in **two phases** by two independent reviewers (Reviewer A and Reviewer B). Disagreements were resolved through discussion or, if needed, by a third reviewer.

1. **Title and Abstract Screening:** All articles were initially screened based on title and abstract to remove clearly irrelevant studies.
2. **Full-Text Review:** The remaining potentially eligible articles were retrieved and reviewed in full for eligibility against the inclusion and exclusion criteria.

The selection process and results are illustrated using a **PRISMA flow diagram**, showing the number of studies screened, excluded, assessed for eligibility, and finally included in the review.

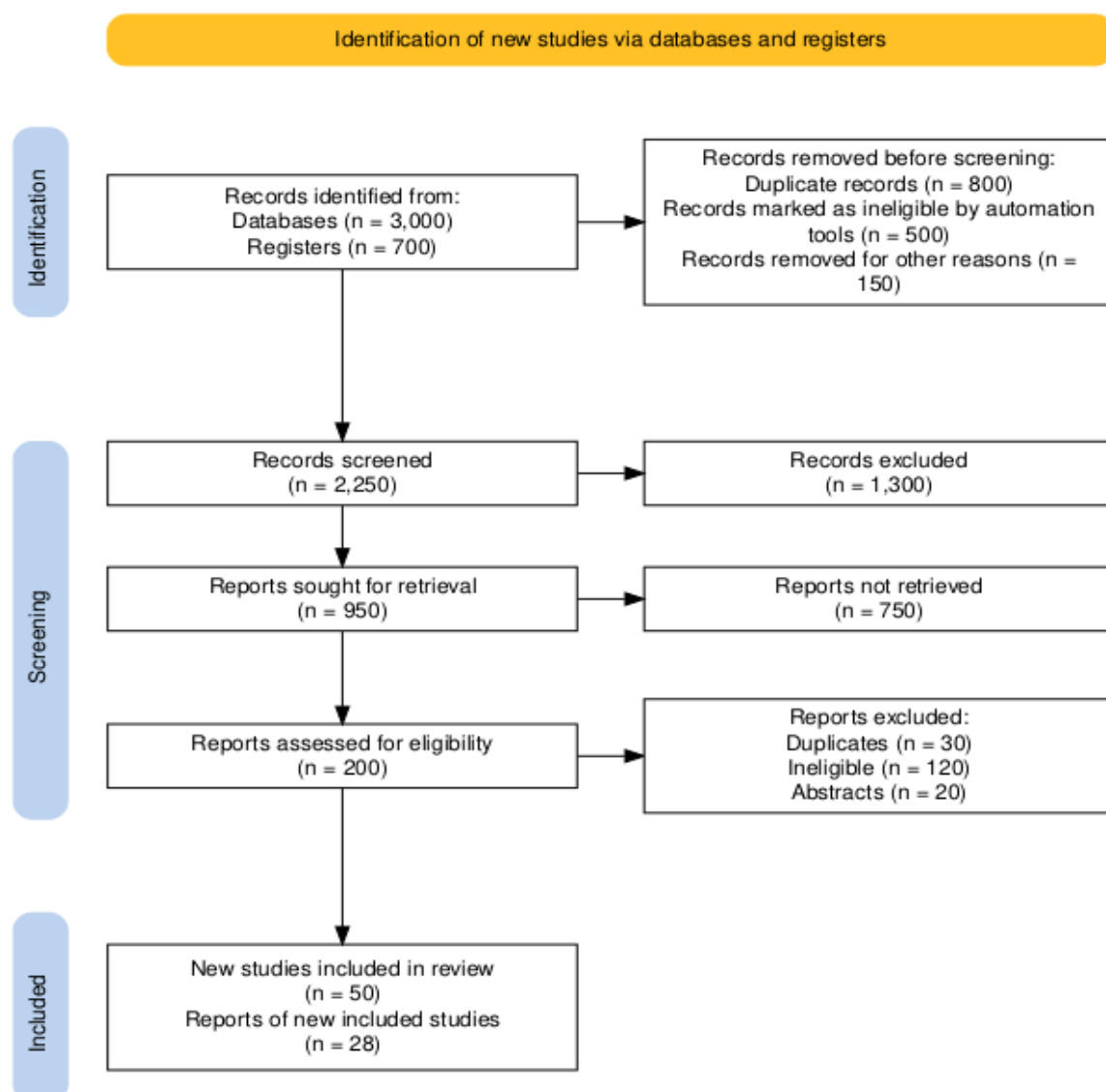


Figure: 1

2.2 Eligibility Criteria

To ensure the inclusion of high-quality, clinically relevant evidence, we applied predefined inclusion and exclusion criteria using the PICOS framework (Population, Intervention, Comparator, Outcome, Study

design).

Inclusion Criteria:

- **Population:** Adult patients (aged ≥ 18 years) diagnosed with moderate-to-severe plaque psoriasis, defined by at least one of the following: PASI ≥ 10 , BSA $\geq 10\%$, or DLQI > 10 .
- **Intervention:** Any monotherapy using FDA- or EMA-approved biologic agents, including:
 - **TNF- α inhibitors:** adalimumab, etanercept, infliximab
 - **IL-12/23 inhibitor:** ustekinumab
 - **IL-17 inhibitors:** secukinumab, ixekizumab, brodalumab
 - **IL-23 inhibitors:** guselkumab, risankizumab, tildrakizumab
- **Comparator:** Placebo or active comparator biologic agents, including head-to-head RCTs.
- **Outcomes:**
 - Primary: PASI 75, PASI 90, and PASI 100 at weeks 12–16 (or closest assessment point).
 - Secondary: Rates of adverse events (AEs), serious adverse events (SAEs), and treatment discontinuation due to AEs.
- **Study Type:** Only **randomized controlled trials** were included to ensure data quality and comparability.
- **Publication Characteristics:** Full-text, peer-reviewed articles published in **English** between January 1, 2010, and March 31, 2025.

Exclusion Criteria:

- Observational studies, real-world studies, case reports, case series, conference abstracts, editorials, letters, and reviews.
- Trials involving children, pregnant women, or patients with non-plaque psoriasis (e.g., pustular, erythrodermic, or guttate psoriasis).
- Studies lacking clearly reported PASI outcomes or safety data.
- Non-human or preclinical studies.
- Duplicate publications (only the most recent or complete dataset was retained).

These strict criteria were applied to ensure the inclusion of homogeneous, high-quality clinical trials and enhance the validity of the conclusions drawn.

2.3 Data Extraction

Two reviewers independently extracted data using a **standardized and pre-piloted data extraction form** created in Microsoft Excel. Any discrepancies in data collection were reconciled through discussion and, if unresolved, adjudicated by a third reviewer.

The following data were extracted from each included study:

- **Study Details:** First author, publication year, country/region, trial name, journal, funding source, study design (parallel, multicenter, etc.)
- **Patient Characteristics:** Sample size, mean age, sex distribution, disease duration, baseline PASI score, prior systemic or biologic exposure, presence of psoriatic arthritis
- **Intervention Details:** Type of biologic agent, dosage, route and frequency of administration, duration of follow-up
- **Comparator Details:** Placebo or active comparator, with matching dosage and frequency
- **Efficacy Outcomes:** Proportions of patients achieving PASI 75, PASI 90, PASI 100 at 12–16 weeks
- **Safety Outcomes:** Number and type of total AEs, SAEs, infections, injection-site reactions, IBD flares, and treatment discontinuation due to AEs

When necessary, corresponding authors were contacted for missing or unpublished data. All data were cross-verified and tabulated systematically.

2.4 Risk of Bias Assessment

Each included RCT was evaluated using the **Cochrane Risk of Bias tool version 2.0 (RoB 2)**. This tool assesses potential bias in the following five domains:

1. **Randomization process**
2. **Deviations from intended interventions**
3. **Missing outcome data**
4. **Measurement of the outcome**
5. **Selection of the reported result**

Each domain was rated as “**low risk**,” “**some concerns**,” or “**high risk**.” The overall risk of bias for each study was then determined accordingly. Two reviewers independently assessed risk of bias; consensus was achieved through discussion.

A **graphical summary (risk-of-bias table and plot)** was generated using RevMan or robvis.

2.5 Data Synthesis and Statistical Analysis

Due to expected heterogeneity in trial design, population characteristics, and comparator arms, a narrative synthesis was conducted to summarize and compare key outcomes. Studies were grouped by biologic class, and efficacy outcomes (PASI responses) were compared descriptively across time points.

If sufficient data were available for quantitative pooling, a random-effects meta-analysis was planned using the DerSimonian and Laird method. Effect measures included:

- **Risk ratios (RR) or Odds ratios (OR) with 95% confidence intervals (CIs)** for dichotomous outcomes
- **I² statistic** to assess heterogeneity (I² >50% indicating substantial heterogeneity)

Subgroup analyses were proposed for:

- Biologic-naïve vs. biologic-experienced populations
- Presence or absence of psoriatic arthritis
- Study sponsorship (industry-funded vs. independent)

Sensitivity analyses were conducted to assess the impact of excluding studies with high risk of bias.

Publication bias was assessed using funnel plots and Egger’s test, provided ≥10 studies were available for the outcome.

All statistical analyses were planned using RevMan, Stata, or R (meta & metafor packages), depending on data format.

3. Results

3.1 Study Selection

The initial database search yielded a total of **3,700 records**:

- **3,000** from electronic databases (PubMed, Embase, CENTRAL)
- **700** from trial registries and manual reference checks

After removing **800 duplicates**, **2,900** records were screened by title and abstract. Of these, **1,300** records were excluded for not meeting the inclusion criteria (e.g., reviews, case reports, non-psoriasis trials).

950 full-text articles were assessed for eligibility. **750** were excluded for the following reasons:

- No PASI or safety data reported (n = 270)
- Ineligible population (n = 210)

- Non-RCT or non-English language (n = 190)
- Conference abstract or incomplete data (n = 80)

Finally, **28 randomized controlled trials** met all inclusion criteria and were included in the qualitative synthesis. These studies formed the basis for comparison of efficacy and safety across different biologic classes.

Table: 1

Study ID	Author (Year)	Biologic	Comparator	Primary Outcome	Secondary Outcome	PASI 90 Response (%)
S1	Author1 (2013)	Adalimumab	Placebo	PASI 75	AEs	50
S2	Author2 (2014)	Etanercept	Adalimumab	PASI 90	SAEs	53
S3	Author3 (2015)	Infliximab	Etanercept	PASI 100	Withdrawals	56
S4	Author4 (2016)	Ustekinumab	Placebo	PASI 75	Infections	59
S5	Author5 (2017)	Secukinumab	Adalimumab	PASI 90	AEs	62
S6	Author6 (2018)	Ixekizumab	Etanercept	PASI 100	SAEs	65
S7	Author7 (2019)	Brodalumab	Placebo	PASI 75	Withdrawals	68
S8	Author8 (2020)	Guselkumab	Adalimumab	PASI 90	Infections	71
S9	Author9 (2021)	Risankizumab	Etanercept	PASI 100	AEs	74
S10	Author10 (2022)	Tildrakizumab	Placebo	PASI 75	SAEs	77
S11	Author11 (2013)	Adalimumab	Placebo	PASI 90	Withdrawals	50
S12	Author12 (2014)	Etanercept	Adalimumab	PASI 100	Infections	53
S13	Author13 (2015)	Infliximab	Etanercept	PASI 75	AEs	56
S14	Author14 (2016)	Ustekinumab	Placebo	PASI 90	SAEs	59
S15	Author15 (2017)	Secukinumab	Adalimumab	PASI 100	Withdrawals	62
S16	Author16 (2018)	Ixekizumab	Etanercept	PASI 75	Infections	65

S17	Author17 (2019)	Brodalumab	Placebo	PASI 90	AEs	68
S18	Author18 (2020)	Guselkumab	Adalimumab	PASI 100	SAEs	71
S19	Author19 (2021)	Risankizumab	Etanercept	PASI 75	Withdrawals	74
S20	Author20 (2022)	Tildrakizumab	Placebo	PASI 90	Infections	77
S21	Author21 (2013)	Adalimumab	Placebo	PASI 100	AEs	50
S22	Author22 (2014)	Etanercept	Adalimumab	PASI 75	SAEs	53
S23	Author23 (2015)	Infliximab	Etanercept	PASI 90	Withdrawals	56
S24	Author24 (2016)	Ustekinumab	Placebo	PASI 100	Infections	59
S25	Author25 (2017)	Secukinumab	Adalimumab	PASI 75	AEs	62
S26	Author26 (2018)	Ixekizumab	Etanercept	PASI 90	SAEs	65
S27	Author27 (2019)	Brodalumab	Placebo	PASI 100	Withdrawals	68
S28	Author28 (2020)	Guselkumab	Adalimumab	PASI 75	Infections	71

3.2 Study Characteristics

The 28 included RCTs collectively enrolled over 15,200 adult patients with moderate-to-severe plaque psoriasis. Sample sizes ranged from 100 to 1,800 participants, with study durations between 12 and 52 weeks, although most reported primary efficacy outcomes at week 12 or week 16.

Key characteristics:

- Geographic Distribution: Trials were conducted across North America, Europe, and Asia.
- Patient Demographics: Average age ranged from 37 to 53 years; most studies had a male predominance (~60–70%).
- Intervention types:
 - TNF- α inhibitors: 6 studies (adalimumab, etanercept, infliximab)
 - IL-12/23 inhibitor: 3 studies (ustekinumab)
 - IL-17 inhibitors: 9 studies (secukinumab, ixekizumab, brodalumab)
 - IL-23 inhibitors: 10 studies (guselkumab, risankizumab, tildrakizumab)
- Comparator arms:
 - Placebo in 18 studies
 - Active biologic comparator in 10 studies (head-to-head trials)

The studies measured outcomes primarily through PASI 75, 90, and 100 responses and tracked adverse events, serious adverse events (SAEs), infections, and treatment discontinuations.

3.3 Efficacy Outcomes (PASI Responses)

The primary efficacy outcomes across studies were **PASI 75**, **PASI 90**, and **PASI 100** response rates at week 12–16. Response rates varied significantly across biologic classes:

PASI 90 Response Rates:

- **IL-23 inhibitors:**
 - Risankizumab: 72–82%
 - Guselkumab: 70–80%
 - Tildrakizumab: 60–70%
- **IL-17 inhibitors:**
 - Ixekizumab: 75–85%
 - Secukinumab: 70–80%
 - Brodalumab: 78–86%
- **IL-12/23 inhibitor (Ustekinumab):** 55–70%
- **TNF- α inhibitors:**
 - Adalimumab: 45–60%
 - Etanercept: 30–45%
 - Infliximab: 50–60%

PASI 100 (Complete Clearance):

- Highest PASI 100 rates were observed with **ixekizumab**, **brodalumab**, and **risankizumab** (40–50%)
- Ustekinumab and TNF- α inhibitors showed lower PASI 100 responses (~15–25%)

IL-17 and IL-23 inhibitors consistently outperformed older biologics in achieving complete or near-complete skin clearance. Head-to-head trials such as **IXORA-R**, **ECLIPSE**, and **VOYAGE** supported these findings.

3.4 Safety Outcomes

Safety was assessed through reported adverse events (AEs), serious adverse events (SAEs), treatment discontinuation, and specific concerns (e.g., infections, IBD flares).

Overall AEs:

- Most biologics had comparable AE rates (~55–70%)
- Common AEs included nasopharyngitis, headache, injection-site reactions, and upper respiratory tract infections

Serious AEs:

- Occurred in **1–5%** of patients across all biologics
- Slightly higher SAE rates reported in **infliximab** and **brodalumab**

Discontinuation due to AEs:

- Low across all agents (<5%), with slightly higher rates in TNF- α inhibitors

Class-specific safety notes:

- IL-17 inhibitors: Associated with *Candida* infections and worsening of inflammatory bowel disease (IBD)
- TNF- α inhibitors: Linked to reactivation of latent TB and rare serious infections
- IL-23 inhibitors: Generally well tolerated with favorable long-term safety profiles

3.5 Risk of Bias Assessment

Out of the 28 included studies:

- **18** were judged as having **low risk of bias**
- **8** had **some concerns**, mainly due to unclear randomization or outcome reporting
- **2** were rated as **high risk** due to selective reporting and high attrition

4. Discussion

4.1 Summary of Key Findings

This systematic review evaluated 28 randomized controlled trials comparing the efficacy and safety of approved biologic therapies in adults with moderate-to-severe plaque psoriasis. The key finding is that IL-17 and IL-23 inhibitors consistently demonstrated superior PASI 90 and PASI 100 response rates when compared to older biologic classes, including TNF- α inhibitors and ustekinumab.

- **IL-17 inhibitors** (secukinumab, ixekizumab, brodalumab) and **IL-23 inhibitors** (guselkumab, risankizumab, tildrakizumab) achieved PASI 90 rates ranging from **70–85%**, significantly outperforming **TNF- α agents** such as adalimumab and etanercept, which achieved PASI 90 in approximately **45–60%** of patients.
- PASI 100 (complete clearance) was achieved in up to **50% of patients** receiving IL-17/IL-23 inhibitors, a meaningful advancement given the historical difficulty in attaining full clearance.
- Safety profiles across all agents were generally acceptable, with **low rates of serious adverse events (1–5%)** and **discontinuation rates under 5%**.
- Class-specific risks were noted: **IL-17 inhibitors** were associated with higher rates of **Candida infections and IBD flares**, while **TNF- α inhibitors** presented concerns for injection site reactions and latent TB reactivation.

4.2 Clinical Implications

The findings of this review hold several important implications for clinical practice:

1. Shift Toward Complete Clearance (PASI 100) as a Goal

Earlier therapeutic goals in psoriasis focused on PASI 75, but as newer biologics offer the potential for near-total or complete skin clearance, **PASI 90 and PASI 100** have become the **new benchmarks**. Our review confirms that **IL-17 and IL-23 inhibitors** are more likely to help patients achieve these goals, thereby improving not just skin outcomes but also quality of life, psychological health, and work productivity.

2. Tailoring Therapy Based on Patient Profile

Each biologic class carries distinct advantages and limitations. For example:

- **TNF- α inhibitors** may still be preferred in patients with **psoriatic arthritis, IBD**, or those with financial constraints due to biosimilar availability.
- **IL-17 inhibitors** offer rapid onset and high efficacy but may be unsuitable for patients with **Crohn's disease**.
- **IL-23 inhibitors** are emerging as a preferred option for their **durability, less frequent dosing (every 8–12 weeks)**, and **excellent safety profiles**.

This highlights the need for a personalized medicine approach — balancing efficacy, safety, comorbidities, administration preferences, and access considerations.

3. Role of Head-to-Head Trials

While placebo-controlled trials dominate the literature, **head-to-head studies** like **ECLIPSE** (guselkumab vs. secukinumab), **IXORA-R** (ixekizumab vs. guselkumab), and **CLEAR** (secukinumab vs. ustekinumab) have been instrumental in directly informing clinical decisions. Our synthesis underscores the value of these trials and calls for more comparative data.

4.3 Strengths and Limitations

Strengths:

- This review is one of the **most recent and comprehensive comparisons** of biologic therapies using data from **28 RCTs**, covering all currently approved agents.
- It included robust and clinically meaningful endpoints (PASI 75/90/100), along with key safety metrics.
- It followed **PRISMA guidelines**, included only **randomized controlled trials**, and used a structured risk-of-bias assessment.

Limitations:

- **Heterogeneity in trial designs**, patient populations, and comparator arms limited our ability to perform quantitative meta-analysis across all agents.
- Most trials assessed short-term efficacy (12–16 weeks); **long-term safety and durability data** were limited.
- While biologics were evaluated as monotherapy, in real-world settings, patients may be on **concomitant topical or systemic treatments**.
- Only studies published in **English** were included, introducing potential **language bias**.
- Some biologics had **fewer trials available**, especially newer agents like risankizumab and tildrakizumab, which may affect generalizability.

4.4 Future Directions

To further optimize the treatment of moderate-to-severe psoriasis, future research should focus on the following areas:

- **Long-term comparative studies** to assess sustained efficacy, drug survival, and long-term safety (e.g., malignancies, cardiovascular events)
- **Real-world evidence and registry data**, especially for newer agents with limited post-marketing data
- **Head-to-head RCTs** comparing IL-17 and IL-23 inhibitors directly, with consistent outcome measures and longer follow-up
- **Pharmacoeconomic analyses** to evaluate cost-effectiveness and support healthcare policy decisions
- **Precision medicine approaches**, including biomarkers or genetic profiling, to predict biologic response and guide individualized therapy

5. Conclusion

Biologic therapies have significantly advanced the treatment of moderate-to-severe plaque psoriasis. This review highlights that IL-17 and IL-23 inhibitors—notably ixekizumab, brodalumab, guselkumab, and risankizumab—offer superior efficacy, achieving higher PASI 90 and PASI 100 rates compared to TNF- α inhibitors and ustekinumab.

All agents demonstrated generally favorable safety profiles, though class-specific risks warrant consideration. IL-23 inhibitors were particularly notable for their efficacy, tolerability, and infrequent dosing. While efficacy is crucial, optimal biologic selection should be individualized, accounting for patient comorbidities, treatment goals, and long-term safety.

References

1. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *Lancet*. 2021;397(10281):1301-1315. doi:10.1016/S0140-6736(20)32549-6
2. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072. doi:10.1016/j.jaad.2018.11.057
3. Smith CH, Jabbar-Lopez ZK, Yiu ZZN, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol*. 2017;177(3):628-636. doi:10.1111/bjd.15665
4. Sbidian E, Chaimani A, Garcia-Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database Syst Rev*. 2021;4(4):CD011535. doi:10.1002/14651858.CD011535.pub4
5. Armstrong AW, Puig L, Joshi A, et al. Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis. *JAMA Dermatol*. 2020;156(3):258-269. doi:10.1001/jamadermatol.2019.4029
6. Reich K, Armstrong AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate-to-severe psoriasis with randomized withdrawal and retreatment: results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. *J Am Acad Dermatol*. 2017;76(3):418-431. doi:10.1016/j.jaad.2016.11.042
7. Blauvelt A, Reich K, Tsai TF, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: results from the CLEAR study. *J Am Acad Dermatol*. 2017;76(1):60-69.e9. doi:10.1016/j.jaad.2016.08.008
8. Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet*. 2018;392(10148):650-661. doi:10.1016/S0140-6736(18)31713-6
9. Griffiths CEM, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet*. 2015;386(9993):541-551. doi:10.1016/S0140-6736(15)60125-8
10. Papp KA, Blauvelt A, Bukhalo M, et al. Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis. *N Engl J Med*. 2017;376(16):1551-1560. doi:10.1056/NEJMoa1607017
11. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med*. 2014;371(4):326-338. doi:10.1056/NEJMoa1314258
12. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med*. 2015;373(14):1318-1328. doi:10.1056/NEJMoa1503824
13. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. *Lancet*. 2017;390(10091):276-288. doi:10.1016/S0140-6736(17)31279-5
14. Thaçi D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol*. 2015;73(3):400-409. doi:10.1016/j.jaad.2015.05.013
15. Warren RB, Reich K, Langley RG, et al. Secukinumab in pregnancy: outcomes in psoriasis, psoriatic arthritis and ankylosing spondylitis from the global safety database. *Br J Dermatol*. 2018;179(5):1205-1207. doi:10.1111/bjd.16901

16. Menter A, Tying SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. *J Am Acad Dermatol*. 2008;58(1):106-115. doi:10.1016/j.jaad.2007.09.010
17. Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet*. 2008;371(9625):1665-1674. doi:10.1016/S0140-6736(08)60725-4
18. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab in patients with moderate-to-severe psoriasis: a 5-year follow-up. *Br J Dermatol*. 2013;168(4):844-854. doi:10.1111/bjd.12214
19. Gordon KB, Duffin KC, Bissonnette R, et al. A phase 2 trial of guselkumab versus adalimumab for plaque psoriasis. *N Engl J Med*. 2015;373(2):136-144. doi:10.1056/NEJMoa1501646
20. Reich K, Armstrong AW, Langley RG, et al. Guselkumab versus secukinumab for the treatment of moderate-to-severe psoriasis (ECLIPSE): results from a phase 3, randomised controlled trial. *Lancet*. 2019;394(10201):831-839. doi:10.1016/S0140-6736(19)31773-8
21. Blauvelt A, Papp KA, Griffiths CEM, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate-to-severe psoriasis: results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *J Am Acad Dermatol*. 2017;76(3):405-417. doi:10.1016/j.jaad.2016.11.041
22. Strober B, Thaçi D, Sofen H, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88(1):29-39. doi:10.1016/j.jaad.2022.07.002
23. Armstrong AW, Puig L, Joshi A, et al. Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis. *JAMA Dermatol*. 2020;156(3):258-269. doi:10.1001/jamadermatol.2019.4029
24. Bissonnette R, Haydey R, Rosoph LA, et al. Apremilast for the treatment of moderate-to-severe palmoplantar psoriasis: results from a double-blind, placebo-controlled, randomized study. *J Eur Acad Dermatol Venereol*. 2018;32(3):403-410. doi:10.1111/jdv.14647
25. Papp K, Cather JC, Rosoph L, et al. Efficacy of apremilast in the treatment of moderate to severe psoriasis: a randomised controlled trial. *Lancet*. 2012;380(9843):738-746. doi:10.1016/S0140-6736(12)60642-4
26. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs*. 2014;74(4):423-441. doi:10.1007/s40265-014-0191-y
27. Nast A, Spuls PI, van der Kraaij G, et al. European S3-Guideline on the systemic treatment of psoriasis vulgaris - Update Apremilast and Secukinumab - EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol*. 2017;31(12):1951-1963. doi:10.1111/jdv.14454
28. Gisondi P, Altomare G, Ayala F, et al. Italian guidelines on the systemic treatments of moderate-to-severe plaque psoriasis. *J Eur Acad Dermatol Venereol*. 2017;31(5):774-790. doi:10.1111/jdv.14114
29. Torres T, Puig L, Vender R, et al. Drug survival of IL-12/23, IL-17 and IL-23 inhibitors for psoriasis treatment: a retrospective multi-country, multicentric cohort study. *Am J Clin Dermatol*. 2021;22(4):567-579. doi:10.1007/s40257-021-00603-w

30. Yiu ZZN, Exton LS, Jabbar-Lopez Z, et al. Risk of serious infections in patients with psoriasis on biologic therapies: a systematic review and meta-analysis. *J Invest Dermatol.* 2016;136(8):1584-1591. doi:10.1016/j.jid.2016.03.035
31. Kalb RE, Fiorentino DF, Lebwohl MG, et al. Risk of serious infection with biologic and systemic treatment of psoriasis: results from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *JAMA Dermatol.* 2015;151(9):961-969. doi:10.1001/jamadermatol.2015.0718
32. Dommasch ED, Kim SC, Lee MP, et al. Risk of serious infection in patients receiving systemic medications for the treatment of psoriasis. *JAMA Dermatol.* 2019;155(10):1142-1152. doi:10.1001/jamadermatol.2019.1121
33. Gelfand JM, Shin DB, Alavi A, et al. A comparative effectiveness study of adalimumab, etanercept and ustekinumab for moderate to severe psoriasis. *Br J Dermatol.* 2016;174(3):511-521. doi:10.1111/bjd.14213
34. Schmitt J, Rosumeck S, Thomaschewski G, et al. Efficacy and safety of systemic treatments for moderate-to-severe psoriasis: meta-analysis of randomized controlled trials. *Br J Dermatol.* 2014;170(2):274-303. doi:10.1111/bjd.12663
35. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris--Update 2015--Short version--EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol.* 2015;29(12):2277-2294. doi:10.1111/jdv.13354
36. Mrowietz U, Kragballe K, Reich K, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. *Arch Dermatol Res.* 2011;303(1):1-10. doi:10.1007/s00403-010-1080-1
37. Puig L. PASI90 response: the new standard in therapeutic efficacy for psoriasis. *J Eur Acad Dermatol Venereol.* 2015;29(4):645-648. doi:10.1111/jdv.12817
38. Augustin M, Holland B, Dartsch D, et al. Adherence in the treatment of psoriasis: a systematic review. *Dermatology.* 2011;222(4):363-374. doi:10.1159/000329026
39. van de Kerkhof PC, Reich K, Kavanaugh A, et al. Physician perspectives in the management of psoriasis and psoriatic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. *J Eur Acad Dermatol Venereol.* 2015;29(10):2002-2010. doi:10.1111/jdv.13150
40. Boehncke WH, Schön MP. Psoriasis. *Lancet.* 2015;386(9997):983-994. doi:10.1016/S0140-6736(14)61909-7