

Update on Biologics for Psoriasis in Clinical Practice

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PRACTICE POINTS

- Choosing a biologic best fit for each patient's individual health profile can reduce psoriasis disease burden.
- Clinicians should educate psoriasis patients that biologics are safe for most comorbidities, and conditions such as obesity have been associated with poorer therapeutic response.
- It is important to discuss possible side effects of biologics with patients and reassure them that mild side effects are the most common during therapy.

Biologics have impacted the clinical management of moderate to severe psoriasis. This review article highlights new data findings from phase 3 clinical trials (N=8) published between May 2020 and February 2021. Data on the efficacy of US Food and Drug Administration–approved biologics for treating psoriasis affirms durable skin clearance in the presence of comorbidities and after treatment gaps. This article aims to provide clinicians with up-to-date knowledge on biologic performance focusing on skin disease clearance, time to skin disease clearance, loss of response and relapse, and treatment-emergent adverse events (TEAEs). Recent trial data in this review focus on treatment with IL-17A inhibitors and IL-23 inhibitors.

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Biologics have transformed the management of moderate to severe psoriasis. There currently are 11 biologics approved by the US Food and Drug Administration (Table) for psoriasis treatment that have been affirmed by various clinical studies. This article provides dosing initiation, maintenance information, and updated clinical data using phase 3 studies (N=8) published between May 2020 and February 2021. Generic names of the 11 biologics were searched separately in the PubMed database within the specified date range. Subsequent results were reviewed by title and selected for phase 3 and 4 trials. Clinical data in this review focus on reducing patient disease burden by allocating a biologic best fit for each patient's individual health profile.

IL-17A Inhibitors Update

Secukinumab is safe and efficacious for skin clearance in the presence of comorbidities and can be used for improving plaque psoriasis and palmoplantar pustular psoriasis. An extension of a phase 3 randomized controlled trial (RCT)—2PRECISE—evaluated the efficacy and safety of secukinumab dosing at 300 mg (n=79) and 150 mg (n=80) in adults with moderate to severe palmoplantar pustular psoriasis (palmoplantar psoriasis area and severity index [PPPASI] score ≥ 12 and dermatology life quality index [DLQI] ≥ 10) over 148 weeks.¹ Extension

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Summary of FDA-Approved Biologics for Psoriasis^a

Biologic	Mechanism of action	Half-life, d	Mode of therapy	Recommended initiation dosing	Recommended maintenance dosing	Recommended dosing adjustments	Recommended time frame to assess for initial therapeutic response, wk
Etanercept	Decoy receptor for soluble TNF- α	3.5	Subcutaneous injection	50 mg twice weekly for 12 consecutive weeks	50 mg once weekly	50 mg twice weekly if poor response	12
Infliximab	Chimeric (mouse + human) monoclonal antibody that binds soluble and transmembrane TNF- α	10	Intravenous infusion	5 mg/kg at wk 0, 2, and 6	5 mg/kg every 8 wk	Up to 10 mg/kg and/or as frequent as every 4 wk if poor response	12
Adalimumab	Human monoclonal antibody that binds soluble and transmembrane TNF- α	14	Subcutaneous injection	80 mg at wk 0, followed by 40 mg at wk 1	40 mg every 2 wk	40 mg once weekly if poor response	12
Certolizumab	Humanized antigen binding monoclonal antibody fragment conjugated with a moiety that binds TNF- α	14	Subcutaneous injection	If ≤ 90 kg: 400 mg at wk 0, 2, and 4; if > 90 kg: 400 mg at wk 0	If ≤ 90 kg: 200 mg every other week; if > 90 kg: 400 mg every 2 wk	NA	12
Ustekinumab	Human monoclonal antibody that binds p40 subunit of IL-12/IL-23	21	Subcutaneous injection	If ≤ 100 kg: 45 mg at wk 0 and 4; if > 100 kg: 90 mg at wk 0 and 4	If ≤ 100 kg: 45 mg every 12 wk; if > 100 kg: 90 mg every 12 wk	Up to 90 mg every 12 wk if ≤ 100 kg or dosing every 8 wk if poor response	12
Secukinumab	Human monoclonal antibody that binds IL-17A	27	Subcutaneous injection	300 mg weekly for 5 consecutive weeks	300 mg every 4 wk	NA	12
Ixekizumab	Humanized monoclonal antibody that neutralizes IL-17A	13	Subcutaneous injection	160 mg at wk 0 followed by 80 mg every 2 wk for 12 consecutive weeks	80 mg every 4 wk	NA	12
Brodalumab	Human monoclonal antibody that binds IL-17A and blocks activity of IL-17A, IL-17F, IL-17A/F, and IL-17E	11	Subcutaneous injection	210 mg at wk 0, 1, and 2	210 mg every 2 wk	NA	12
Guselkumab	Human monoclonal antibody that blocks p19 subunit of IL-23	18	Subcutaneous injection	100 mg at wk 0 and 4	100 mg every 8 wk	NA	12
Tildrakizumab	Humanized monoclonal antibody that blocks p19 subunit of IL-23	23	Subcutaneous injection	100 mg at wk 0 and 4	100 mg every 12 wk	NA	12
Risankizumab	Humanized monoclonal antibody that binds p19 subunit of IL-23	28	Subcutaneous injection	150 mg (two 75-mg injections) at wk 0 and 4	150 mg every 12 wk	NA	12

Abbreviations: FDA, US Food and Drug Administration; TNF, tumor necrosis factor; NA, not applicable.

^aAs of July 2021.

patients were included from the 52-week 2PRECISE study per the investigator's judgement of a meaningful clinical response (exact criteria not described). All treatment groups demonstrated a mean (SD) PPPASI of 22.7 (9.5) by the extension trial's start. Results affirmed that clinical response waned after week 148 in all groups excluding placebo/secukinumab 150 mg, which maintained a mean (SD) PPPASI of 22.7 (9.5). The most frequent adverse events were nasopharyngitis, pustular psoriasis, headache, and pruritus.¹

Comorbidities do not have a major impact on secukinumab's efficacy. A post hoc analysis of 4 phase 3 RCTs—ERASURE, FIXTURE, FEATURE, and JUNCTURE—gathered data from adult patients (N=2401) to assess baseline comorbidities with efficacy and safety of secukinumab vs etanercept after 12 weeks of treatment.² Sixty-one percent (n=1469) had at least 1 comorbidity, most frequently obesity, hypertension, psoriatic arthritis, hyperlipidemia, or diabetes mellitus. All patient groups had a greater likelihood of a psoriasis area and severity index (PASI) response with any dose of secukinumab vs patients with comorbidities who were taking etanercept or placebo ($P<.05$) at week 12. All groups had a greater likelihood of achieving investigator global assessment scores of 0/1 (clear/almost clear) vs patients with comorbidities taking etanercept or placebo ($P<.05$). Baseline comorbidities did not significantly affect treatment response, except obesity, which was associated with decreased probability of achieving all PASI and investigator global assessment ($P<.01$) responses. Secukinumab-treated patients with and without comorbidities had equivalent likelihood of treatment-emergent adverse events (TEAEs).²

Brodalumab is an effective biologic that has shown long-term safety with continuous administration. Continuous brodalumab and brodalumab after placebo demonstrated impactful skin clearance after 120 weeks in AMAGINE-1, a phase 3 RCT involving adults (N=442) with moderate to severe plaque psoriasis.³ Patients randomized to brodalumab 210 mg (n=222) or placebo (n=220) were rerandomized according to initial treatment response. In patients switching from brodalumab to placebo at week 12, 55% and 94% achieved PASI 75 at week 20 and week 120, respectively, and 75% reached PASI 100 at week 120. Of patients with static physician global assessment (sPGA) scores of 0/1 (clear/almost clear) at week 12 who were rerandomized to brodalumab, 96% and 80% (using observed data) achieved PASI 75 and PASI 100, respectively. Mean (SD) time to return of skin disease following withdrawal of brodalumab was 74.7 (50.5) days. Treatment-emergent adverse events included headaches, arthralgia, diarrhea, and nausea. Suicidal ideation was rare (this study had 1 completed suicide), and authors cited that no causal association has been made between brodalumab and suicidality. Brodalumab also demonstrated favorable treatment response in patients who underwent a lapse in treatment, offering real-world

value, as intermittent treatment administration can occur because of personal or financial reasons.³

Ixekizumab is associated with more rapid skin clearance, better resolution of nail psoriasis, and superior improvement in quality-of-life measures when compared with guselkumab. The phase 3 study IXORA-R compared skin and nail clearance as well as patient-reported outcomes over 24 weeks with ixekizumab 80 mg (n=520) vs guselkumab 100 mg (n=507) in adults with moderate to severe plaque psoriasis.⁴ Ixekizumab (50%) was shown to be no worse than guselkumab (52%; difference, -2.3%) using a noninferiority test (noninferiority margin of -11.4%). The treatments exhibited similar efficacy, with no significant difference in proportion of patients reaching PASI 100 ($P=.41$). Ixekizumab patients tended to have skin clearance sooner than guselkumab patients, reaching PASI 50/75/90 and PASI 100 in a median time that was 2 weeks and 7.5 weeks earlier, respectively. More ixekizumab patients (52%) achieved clear nails vs guselkumab patients (31%; $P=.007$). Ixekizumab patients reported greater satisfaction with their skin disease affecting quality of life (DLQI), with more DLQI 0/1 (no effect at all on patient's life) scores and being itch free ($P<.05$). Ixekizumab was associated with significantly more days of complete skin clearance (PASI 100) vs guselkumab (55.6 days vs 42.2 days; $P<.001$). Although an upper respiratory tract infection was the most common TEAE, the proportion of TEAEs was similar between treatments.⁴

IL-23 Inhibitors Update

Tildrakizumab has similar long-term skin clearance efficacy and safety in patients with psoriasis with and without comorbid metabolic syndrome (MetS). A post hoc analysis of 2 phase 2 RCTs (reSURFACE 1/2) involving adults (N=338 and N=307) with moderate to severe plaque psoriasis assessed long-term efficacy (3 years), drug survival, and safety for 5 years of continuous tildrakizumab 100 mg and 200 mg in adults with comorbid MetS.⁵ Although no difference in efficacy was concluded, greater body mass index of the MetS population was shown to be associated with lower biologic efficacy compared to the general population. The proportion of patients who achieved PASI 75 at week 52 was comparable in patients with MetS and patients without MetS (tildrakizumab 100 mg, 85% and 86% vs 86% and 94% for reSURFACE 1/2, respectively; tildrakizumab 200 mg, 76% and 87% vs 76% and 87% for reSURFACE 1/2, respectively).⁵

Tildrakizumab also demonstrated efficacy and safety for up to 5 years in 2 other phase 3 RCTs with no dose-related differences in frequency of injections and malignancies. Tildrakizumab 100 mg is the recommended dose. The 200-mg dose can be utilized in patients with a high burden of disease and disability. reSURFACE 1 and reSURFACE 2 involved adults with chronic moderate to severe plaque psoriasis randomized to tildrakizumab 100 mg, 200 mg, or placebo with the option of long-term extension to week 244 if patients reached 50% or greater improvement

from baseline PASI score.⁶ Patients in reSURFACE 2 also were randomized to etanercept 50 mg with partial responders and nonresponders at week 28 switching to tildrakizumab 200 mg until week 244. Extension results showed PASI 75 achievement in 88.7% (95% CI, 84.6%-92.1%) of patients taking tildrakizumab 100 mg (n=235), 92.5% (95% CI, 88.1%-95.7%) of patients taking tildrakizumab 200 mg (n=176), and 81.3% (95% CI, 72.6%-88.2%) of patients taking etanercept/partial nonresponders (n=85). The most common TEAE was nasopharyngitis (10.5/100 patient-years for tildrakizumab 100 mg and 10.7/100 patient-years for tildrakizumab 200 mg). The frequency of severe infections (eg, diverticulitis, pneumonia, cellulitis, appendicitis) was 1.2 per 100 patient-years for tildrakizumab 100 mg and 1.3 per 100 patient-years for tildrakizumab 200 mg.⁶

Risankizumab and tildrakizumab require the lowest number of injections, thereby providing sustainable skin clearance with a convenient injection dosing schedule for patients. Risankizumab efficacy (8.2% with inferiority margin of 12%) was noninferior to secukinumab when assessing the proportion of PASI 90 responders at week 16 (after 2 doses of risankizumab vs 7 doses of secukinumab).⁷ IMMerge, an international phase 3 RCT, involved adults (N=327) with moderate to severe plaque psoriasis to compare the safety and efficacy of risankizumab 150 mg (n=164) vs secukinumab 300 mg (n=163) up to 52 weeks. A greater proportion of the risankizumab arm (86.6%) achieved PASI 90 in 52 weeks compared to the secukinumab arm (57.1%). Superior skin clearance (PASI 90) at week 52 was achieved after 5 doses with risankizumab vs 16 doses of secukinumab. Risankizumab TEAEs were nasopharyngitis, upper respiratory tract infection, headache, arthralgia, diarrhea, and bronchitis.⁷

Continuous risankizumab treatment shows substantially stronger skin clearing performance compared with intermittent treatment following drug withdrawal, demonstrating that treatment gaps minimize therapeutic response. IMMhance, an international phase 3 RCT involving adults (N=507) with moderate to severe plaque psoriasis, evaluated the safety and efficacy with risankizumab 150 mg after 52 weeks and 104 weeks.⁸ Part A randomized patients to risankizumab 150 mg (n=407) or placebo (n=100). Part B rerandomized patients at week 28 to continue risankizumab 150 mg or placebo (designated as withdrawal of treatment; later re-treated with risankizumab 150 mg if patients had sPGA ≥ 3). At week 52, significantly more patients reached sPGA score of 0/1 with risankizumab/risankizumab (n=97 [87.4%]) vs risankizumab/placebo (n=138 [61.3%]; $P < .001$). At week 104, significantly more patients reached an sPGA score of 0/1 with risankizumab/risankizumab

(n=90 [81.1%]) vs risankizumab/placebo (n=16 [7.1%]; $P < .001$). Risankizumab exhibited longevity following withdrawal, as median time to loss of response and relapse was 42 weeks (sPGA ≥ 3). The extent of TEAEs was similar between risankizumab and placebo and included nasopharyngitis, upper respiratory tract infection, headache, and back pain.⁸

Final Thoughts

Biologics for psoriasis help produce intended results for skin disease clearance and are tools for precision medicine. Recent data demonstrate safe, durable, and continuous efficacy with biologics, which offer patients a better chance of treatment success. This guide may serve as a quick reference for biologic selection with special consideration of individual disease characteristics and comorbidities.

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