Review of bimekizumab in the treatment of psoriasis

Sindhuja Koppu, Rohan Singh, Kiranjit Kaur, and Steven R. Feldman

ABSTRACT
Bimekizumab, a selective interleukin (IL) 17 inhibitor, is an emerging systemic treatment for moderate-to-severe psoriasis. Although IL-19, IL-22, and IL-36 are implicated in the pathogenesis of psoriasis, IL-17 drives the activation of these interleukins and the formation of psoriatic plaques. This review assesses the efficacy, safety, and implications of bimekizumab in the treatment of moderate-to-severe psoriasis. A review of literature was conducted using the PubMed repository in March 2022. Articles in English discussing the use of bimekizumab in the treatment of psoriasis were included. One phase II and four phase III trials were included. During clinical trials, bimekizumab was more efficacious, when compared to placebo, ustekinumab, adalimumab, and secukinumab in the treatment of moderate to severe psoriasis. Bimekizumab is a promising, efficacious, and relatively tolerable emerging systemic treatment for moderate-to-severe plaque psoriasis.

Introduction
Psoriasis is a chronic, systemic inflammatory skin disease that is associated with psoriatic arthritis, cardiovascular disease, obesity, diabetes mellitus, and bowel disease. Psoriasis affects approximately 125 million people worldwide and 7.5 million people in the United States and most commonly presents in the skin as plaque psoriasis, which comprises 80% of cases.

Over the past two decades, increased understanding of the underlying molecular pathogenesis of psoriasis has facilitated the development of targeted systemic treatments, particularly in the form of biologics. Currently, there are 11 FDA approved biologics for the treatment of psoriasis. Bimekizumab is currently undergoing clinical trials for the treatment of moderate-to-severe psoriasis. If approved, bimekizumab will be the fourth IL-17 inhibitor approved for this cause. Furthermore, it would be the first IL-17 inhibitor to target both IL-17A and IL-17F.

This narrative review will summarize the nature of psoriasis, bimekizumab’s basis in psoriatic pathophysiology, as well as its efficacy, safety, and implications for the treatment of moderate-to-severe plaque psoriasis.

Methods
The aim of this study was to conduct a product review on the use of bimekizumab in treatment of psoriasis. This review considers the advantages, disadvantages, mechanism of action, intended use, clinical efficacy, and regulatory issues of bimekizumab. Review of literature was conducted using the MEDLINE (PubMed) database in early March of 2022 using the terms “bimekizumab” and “psoriasis.” A total of 52 articles were identified and peer-reviewed preclinical and clinical trials in English discussing the use of bimekizumab in the treatment of psoriasis published between the years 2008 to 2021 were included. One phase IIb trial and four phase III trials were included. References from included articles were searched for relevant citations.

Nature of the disease
Psoriasis is a chronic systemic inflammatory disease which most commonly presents in the skin as psoriasis vulgaris or plaque psoriasis. Plaque psoriasis clinically manifests as erythematous plaques with silver scales on extensor surfaces, trunk, and scalp. Other cutaneous manifestations of psoriasis include inverse or flexural psoriasis, which presents without scaling and affects axillary, inframammary, and genital areas, guttate psoriasis, which presents as papules and plaques that resemble drops involving the trunk and limbs, and erythrodermic psoriasis, which is a life-threatening condition that presents as a diffuse erythematous rash. Psoriasis is also associated with other comorbidities such as cardiovascular, gastrointestinal, and renal diseases. Other diseases such as mood disorders, inflammatory arthritis, malignancy, and infections are prevalent in patients with psoriasis. Psoriatic arthritis is prevalent in approximately 20–30% of patients with psoriasis and is an inflammatory musculoskeletal disease that affects multiple axial and peripheral joints as well as skin and nails.

Basis in pathology
Psoriasis is a chronic inflammatory disease which leads to uncontrolled keratinocyte differentiation and proliferation.
Injury to keratinocytes causes release of antimicrobial peptides (AMPs), which act on dendritic cells. IL-37, an AMP, activates plasmacytoid dendritic cells, which subsequently produce type I interferons. Type I interferons such as IFN-α and IFN-β cause myeloid dendritic cells (mDCs) to active type I helper T cells (Th1) and type 17 helper T cells (Th17). Th1 cells produce IFN-γ, and Th17 cells produce IL-17, IL-22, and TNF-α. IL-17 is crucial to the pathogenesis of psoriatic plaques as it causes expression and release of many proteins from keratinocytes that cause psoriasis, including S100 proteins, IL-37/cathelicidin, hBD2, and LCN2. IL-17 also activates CCAAT enhancer-binding protein (C/EBPβ and δ), STAT1, and nuclear factor κB (NF-κB), which help drive plaque formation as well as IL-19, IL-22, and IL-36 which lead to epidermal hyperplasia.

IL-17 inhibitors

IL-17 is a family of cytokines which consist of six structurally similar members: IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F. IL-17 is a major cytokine in the pathogenesis of psoriasis and multiple biologics selectively target IL-17. These include secukinumab, ixekizumab, and brodalumab, and most recently bimekizumab.

Preclinical studies

Initially, 496.g1 was identified as a humanized antibody with a strong affinity for IL-17A but had a weak affinity for IL-17F. To increase the selectivity of 496.g1, affinity maturation was performed to convert it to 496.g3. 496.g3 had a strong affinity for both IL-17A and IL-17F, with Kd values (affinity constants) of 3.2pM and 23pM, respectively, and was renamed as bimekizumab.

| Table 1. Efficacy results from phase II and III clinical trials. |
|---------------------------------------------------------------|
| **Trial** | **Primary Endpoint** | **Treatment Duration** | **Treatment Groups (% Achieving)** |
| Phase IIb (BE ABLE) | PASI 90 | 12 weeks | Bimekizumab Q4W | Placebo Q4W |
| | | | 64 mg: 46.2% | 160 mg: 67.4% | 0% |
| | | | 160 mg with 320 mg loading dose: 75% |
| | | | 320 mg: 79.1% |
| Phase III (BE VIVID) | PASI90 | 16 weeks | Bimekizumab Q4W | Placebo |
| | | | 320 mg: 85% |
| | IGA 0/1 | 16 weeks | 320 mg: 84% |
| | | | 5% |
| Phase III (BE READY) | PASI90 | 16 weeks | Bimekizumab Q4W | Placebo |
| | IGA 0/1 | 16 weeks | 320 mg: 91% |
| | | | 320 mg: 93% |
| | | | 1% |
| Phase III (BE SURE) | PASI90 | 16 weeks | Bimekizumab Q4W | Adalimumab Q2W |
| | IGA0/1 | 16 weeks | 320 mg: 86.2% | 40 mg: 47.2% |
| | | | 40 mg: 57.2% |
| Phase III (BE RADIAN) | PASI90 | 16 weeks | Bimekizumab Q4W | Secukinumab Q1W(week 4) |
| | | | 320 mg: 61.7% | then Q4W |
| | PASI100 | 48 weeks | 320 mg: 67.0% | 300 mg: 48.9% |
| | | | 300 mg: 46.2% |

Clinical studies

**Phase II studies**

A randomized, double-blinded, multicenter, placebo-controlled phase IIb trial (BE ABLE: NCT02905006) evaluated the safety and efficacy of bimekizumab in 250 adult participants with moderate-to-severe plaque psoriasis at baseline with Psoriasis Area and Severity Index (PASI) score ≥12, ≥10% body surface area (BSA) involvement, and Investigator’s Global Assessment (IGA) score ≥3 for ≥6 months. All participants received bimekizumab every 4 weeks (Q4W) at doses of 64 mg, 160 mg, 160 mg with 320 mg loading dose, 320 mg, 480 mg, or placebo Q4W. The primary endpoint was the percentage who achieved 90% improvement in PASI score (PASI90) after 12 weeks of treatment. After 12 weeks of treatment, more participants in the bimekizumab groups (64 mg: 46.2%, 160 mg: 67.4%, 160 mg with a 320 mg loading dose: 75.00%, 320 mg: 79.1%, and 480 mg: 72.1%) achieved PASI90 compared to placebo (0%, p < .0001 for all doses) (Table 1).

**Phase III studies**

A randomized, double-blinded, multicenter, phase III trial (BE VIVID: NCT03370133) evaluated the safety and efficacy of bimekizumab in 567 adult participants with moderate to severe plaque psoriasis at baseline for at least 6 months with PASI ≥12, ≥10% BSA involvement, and IGA ≥3. Participants received bimekizumab 320 mg Q4W, ustekinumab 45 mg or 90 mg (based on weight) at weeks 0 and 4 then every 12 weeks (Q12W), or placebo Q4W. The primary endpoints were the percentage with PASI90 and an IGA response of clear (score 0) or almost clear (score 1) after 16 weeks of initial treatment. At week 16, more participants treated with bimekizumab (85%) achieved PASI90, versus either ustekinumab or placebo (50% and 15%, respectively; p < .0001 for both). More participants

Abbreviations: IGA 0/1 – Investigator’s Global Assessment response of clear (score 0) or almost clear (score 1); PASI90 – 90% improvement or more from baseline on Psoriasis Area and Severity Index; PASI100 – 100% improvement or more from baseline on Psoriasis Area and Severity Index, DBPC – Double Blind Placebo Controlled, DB – Double Blind, Q2W – every two weeks, Q4W – every four weeks, Q8W – every eight weeks, Q12W – every twelve weeks.
treated with bimekizumab achieved IGA success (84%), versus ustekinumab and placebo (53% and 5%, respectively; p < .0001 for both).12 Weeks 16–52 were part of the maintenance treatment period. After 16 weeks, participants in the placebo group were switched to receive bimekizumab 320 mg Q4W up to week 52, and the participants in the other treatment groups continued their original treatment. At week 52, more participants treated with bimekizumab (65%) achieved PASI100 compared to ustekinumab (38%, p < .0001) (Table 1).12

A randomized, double-blinded, multicenter, placebo-controlled, phase III trial (BE READY: NCT03410992) evaluated the safety and efficacy of bimekizumab in 435 adult participants with moderate to severe plaque psoriasis for at least 6 months with PASI ≥12, ≥10% BSA, and IGA ≥3.13 Participants received either bimekizumab 320 mg or placebo Q4W. The primary endpoints were the percentage that achieved PASI90 and IGA 0/1 after 16 weeks of treatment. At week 16, more participants treated with bimekizumab achieved PASI90 (91%) and IGA success (93%), versus placebo (1% for both; p < .0001 for both).13 Also at week 16, participants who were treated with bimekizumab and achieved PASI90 were re-assigned in a 1:1 manner to receive bimekizumab 320 mg Q4W, every 8 weeks (Q8W), or placebo until week 56. At week 56, PASI90 was maintained by 87% of the participants assigned to bimekizumab Q4W, by 91% of the participants assigned to bimekizumab 320 mg Q8W, and by 16% of the participants assigned to the placebo group (Table 1).13

A randomized, double-blinded, multicenter, phase III trial (BE SURE: NCT03412747) evaluated the safety and efficacy of bimekizumab in 478 adult participants with moderate to severe plaque psoriasis for at least 6 months with PASI ≥12, ≥10% BSA, and IGA ≥3.14 Participants received either bimekizumab 320 mg Q4W for 56 weeks, bimekizumab 320 mg Q4W for 16 weeks, then Q8W for weeks 16–56, or adalimumab 80 mg at baseline, 40 mg 1 week later, then 40 mg Q2W for 24 weeks and were then switched to bimekizumab 320 mg Q4W to week 56. The primary endpoints were the percentage who achieved PASI90 and IGA score of 0/1 after 16 weeks of treatment.14 At week 16, more participants treated with bimekizumab (86.2%, pooled analysis) achieved PASI90, versus adalimumab (47.2%, p < .0001). In addition, at week 16, more participants treated with bimekizumab (85.3%, pooled analysis) achieved IGA score of 0/1, versus adalimumab (57.2%, p < .0001).14 At week 56, 81.8% of the participants in the adalimumab group who switched to bimekizumab at week 24 achieved PASI90 (Table 1).14

A randomized, double-blinded, multicenter, phase IIIb trial (BE RADIANT: NCT03536884) evaluated the safety and efficacy of bimekizumab in 743 adult patients with moderate-to-severe plaque psoriasis for at least 6 months with PASI ≥12, ≥10% BSA, and IGA ≥3.15 Participants received either bimekizumab 320 mg Q4W or secukinumab 300 mg weekly to week 4, followed by Q4W to week 48. The primary endpoint was the percentage who achieved PASI100 after 16 weeks of treatment.15 At week 16, more participants treated with bimekizumab (61.7%) achieved PASI100, versus secukinumab (48.9, p < .0001). Also, at week 16, participants in the bimekizumab group underwent 1:2 randomization to receive bimekizumab 320 mg Q4W or bimekizumab 320 mg Q8W to week 48 while the participants in the secukinumab group continued their original treatment. At week 48, more participants treated with bimekizumab Q4W and Q8W (67.0%) achieved PASI100, versus secukinumab (46.2%, p < .0001) (Table 1).15

Safety

In the phase IIIb (BE ABLE, NCT02905006) trial, participants who received bimekizumab experienced adverse events (AEs) more frequently at week 12 (64 mg: 69.2%, 160 mg: 55.8%, 160 mg with 320 mg loading dose: 60.0%, 320 mg: 60.5%, and 480 mg: 58.1%), versus placebo (55.7%). The most common AEs in the bimekizumab 64 mg, 160 mg, 160 mg with 320 mg loading dose, 320 mg, and 480 mg groups were nasopharyngitis (12.8%, 7.0%, 7.5%, 14.0%, 9.3%, respectively), upper respiratory tract infections (12.8%, 4.7%, 7.5%, 4.7%, 0%), and arthralgias (5.1%, 0%, 2.5%, 2.3%, 7.0%), which occurred at higher rates compared to placebo (4.8%, 2.4%, and 0%, respectively) (Table 2).11

In the phase III (BE VIVID, NCT03370133) trial, participants who received bimekizumab (56%) experienced AEs at a similar rate to ustekinumab (51%) and placebo (47%) during the initial treatment period from weeks 0–16.12 In participants who received bimekizumab between weeks 0–16, the most common AEs were nasopharyngitis (9%), oral candidiasis (9%), and upper respiratory tract infections (3%). During the initial and maintenance periods from weeks 0–52, the most common AEs in the bimekizumab group were nasopharyngitis (22%), oral candidiasis (15%), and upper respiratory tract infections (9%) (Table 2).12

In the phase III (BE READY, NCT03410992) trial, participants who received bimekizumab (61%) experienced AEs more frequently, versus placebo (41%) during the initial treatment period from weeks 0–16. In participants who received bimekizumab between weeks 0–16, the most common AEs were nasopharyngitis (7%), oral candidiasis (6%), and upper respiratory tract infections (4%).13 In the randomized withdrawal period from weeks 16–56, participants who received bimekizumab experienced AEs (320 mg Q8W: 77% and 320 mg Q4W: 74%) at a similar rate to placebo (69%). The most common AEs experienced by participants treated with bimekizumab 320 mg Q8W and Q4W during the randomized withdrawal period were nasopharyngitis (23% and 10%), oral candidiasis (9% and 11%), and upper respiratory tract infections (8% and 11%), respectively (Table 2).13

In the phase III (BE SURE, NCT03412747) trial, participants who received bimekizumab experienced AEs (Q4W: 70.9%, Q4W and then switched to Q8W: 72%) at a similar frequency versus adalimumab (69.8%) during treatment weeks 0–24.14 The most frequent AEs experienced by participants who received bimekizumab Q4W and those who received Q4W and then switched to Q8W were upper respiratory tract infections (30.4% and 28.0%), oral candidiasis (9.5% and 11.8%), hypertension (3.8% and 5.6%), and diarrhea (5.1% and 3.1%), respectively. During weeks 24–56, the most frequent AEs were upper respiratory tract infections (23.7% and 24.2%), oral candidiasis (13.2% and 8.7%), hypertension (1.3% and 2.0%), and diarrhea (1.3% and 2.0%) for bimekizumab.
Table 2. Overview of the safety data of phase II and III trials for bimekizumab.

| Trial                     | Duration | Treatment Groups (% Adverse Effects) |
|---------------------------|----------|-------------------------------------|
| Phase IIb (BE ABLE)       | 12 Weeks | Bimekizumab 64 mg:                  |
|                           |          | Total Incidence: 69.2%              |
|                           |          | Nasopharyngitis: 12.8%              |
|                           |          | URI: 12.8%                          |
|                           |          | Arthralgias: 5.1%                   |
|                           |          | 160 mg:                             |
|                           |          | Total Incidence: 55.8%              |
|                           |          | Nasopharyngitis: 7.0%               |
|                           |          | URI: 4.7%                           |
|                           |          | Arthralgias: 0%                     |
|                           |          | 160 mg w 320 mg LD                  |
|                           |          | Total Incidence: 60.0%              |
|                           |          | Nasopharyngitis: 7.5%               |
|                           |          | URI: 7.5%                           |
|                           |          | Arthralgias: 2.5%                   |
|                           |          | 320 mg:                             |
|                           |          | Total Incidence: 60.9%              |
|                           |          | Nasopharyngitis: 14.0%              |
|                           |          | URI: 4.7%                           |
|                           |          | Arthralgias: 2.3%                   |
|                           |          | 480 mg:                             |
|                           |          | Total Incidence: 58.1%              |
|                           |          | Nasopharyngitis: 9.3%               |
|                           |          | URI: 0%                             |
|                           |          | Arthralgias: 7.0%                   |
| Phase III (BE VIVID)      | Weeks 0-16| Bimekizumab                          |
|                           |          | Total Incidence: 56%                |
|                           |          | Nasopharyngitis: 9%                 |
|                           |          | Oral Candidiasis: 9%                |
|                           |          | URI: 3%                             |
|                           |          | Placebo                             |
|                           |          | Total Incidence: 47%                |
|                           |          | Nasopharyngitis: 8%                 |
|                           |          | Oral Candidiasis: 0%                |
|                           |          | URI: 2%                             |
|                           |          | Ustekinumab                          |
|                           |          | Total Incidence: 51%                |
|                           |          | Nasopharyngitis: 9%                 |
|                           |          | Oral Candidiasis: 0%                |
|                           |          | URI: 3%                             |
|                           |          | Total Incidence: 80%                |
|                           |          | Nasopharyngitis: 22%                |
|                           |          | Oral Candidiasis: 1%                |
|                           |          | URI: 11%                            |
| Phase III (BE READY)      | Weeks 0-16| Bimekizumab                          |
|                           |          | Total Incidence: 61%                |
|                           |          | Nasopharyngitis: 7%                 |
|                           |          | Oral Candidiasis: 6%                |
|                           |          | URI: 4%                             |
|                           |          | Placebo                             |
|                           |          | Total Incidence: 41%                |
|                           |          | Nasopharyngitis: 5%                 |
|                           |          | Oral Candidiasis: 0%                |
|                           |          | URI: 8%                             |
|                           | RWP      | 320 mg Q8W:                          |
|                           | Weeks 16-56 | Total Incidence: 77%              |
|                           |          | Nasopharyngitis: 23%                |
|                           |          | Oral Candidiasis: 9%                |
|                           |          | URI: 8%                             |
|                           |          | 320 mg Q4W:                          |
|                           |          | Total Incidence: 74%                |
|                           |          | Nasopharyngitis: 10%                |
|                           |          | Oral Candidiasis: 11%               |
|                           |          | URI: 11%                            |
| Trial                        | Duration | Treatment Groups (% Adverse Effects)                                                                 |
|-----------------------------|----------|-----------------------------------------------------------------------------------------------------|
| Phase III (BE SURE)         | Weeks 0-24 | Bimekizumab  
Q4W:  
Total Incidence: 70.9%  
URI: 30.4%  
Oral Candidiasis: 9.5%  
HTN: 3.8%  
Diarrhea: 5.1%  
Q4W switched to Q8W:  
Total Incidence: 72%  
URI: 28.0%  
Oral Candidiasis: 11.8%  
HTN: 5.6%  
Diarrhea: 3.1%  
Adalimumab  
Total Incidence: 69.8%  
URI: 34.6%  
Oral Candidiasis: 0%  
HTN: 8.2%  
Diarrhea: 2.5% |
|                             | Weeks 24-56 | Bimekizumab  
Q4W:  
Total Incidence: 66.4%  
URI: 23.7%  
Oral Candidiasis: 13.2%  
HTN: 1.3%  
Diarrhea: 1.3%  
Q4W switched to Q8W:  
Total Incidence: 69.8%  
URI: 24.2%  
Oral Candidiasis: 8.7%  
HTN: 2.0%  
Diarrhea: 2.0%  
Adalimumab→  
Bimekizumab  
Q4W:  
Total Incidence: 74.5%  
URI: 28.2%  
Oral Candidiasis: 17.4%  
HTN: 2%  
Diarrhea: 1.3% |
| Phase III (BE RADIANT)      | Weeks 0-48 | Bimekizumab  
Total Incidence: 86.1%  
URI: 38.9%  
Oral Candidiasis: 19.3%  
UTI: 6.7%  
Q4W:  
Total Incidence: 81.0%  
Q8W:  
Total Incidence: 75.3%  
Secukinumab  
Total Incidence: 81.4%  
URI: 41.6%  
Oral Candidiasis: 3%  
UTI: 5.9% |
|                             | Weeks 16-48 |                                                                                                      |

Abbreviations: URI – Upper Respiratory Infection, UTI – Urinary Tract Infection, LD – Loading Dose, RWP – Randomized Withdrawal Period, HTN – Hypertension, Q8W – every eight weeks, Q4W – every four weeks.
Q4W and bimekizumab Q4W followed by Q8W, respectively (Table 2).

In the phase III (BE RADIANT: NCT03536884) trial, participants who received bimekizumab experienced a similar rate of AEs (86.1%) as those who received secukinumab (81.4%) during weeks 0–48. The most common AEs in the bimekizumab group were upper respiratory tract infections (38.9%), oral candidiasis (19.3%), and urinary tract infection (6.7%). Similarly, participants who received bimekizumab Q4W experienced a similar rate of AEs (81.0%), compared to participants who received bimekizumab Q8W (75.3%) from weeks 16–48 (Table 2).

Public health implications

Most patients with psoriasis are predisposed to a decreased quality of life and psychiatric comorbidities such as depression, anxiety, and suicidal ideation. Specifically, up to 20% of psoriatic patients may have concurrent depression. The visual manifestations of psoriasis may also lead to social discrimination, negatively impacting patient interpersonal relationships.

Despite the development of numerous biologics targeting psoriasis’ pathogenesis, some patients may be resistant to treatment or develop resistance to treatment. Patients may also experience psoriatic flares after withdrawing from treatment with biologics. Bimekizumab offers an additional biologic to provide patients with a targeted, efficacious, and relatively tolerable treatment alternative.

Product availability

Several phase III trials have been conducted studying bimekizumab, and patients who completed these studies are currently being enrolled in an open-label trial (BE BRIGHT) to assess the efficacy, safety, and tolerability of bimekizumab for 144 weeks. Since September 2020, bimekizumab is being reviewed by the Food and Drug Administration (FDA) and European Medicines Agency (EMA) for the treatment of psoriasis. Bimekizumab is currently not FDA approved but is being studied for psoriatic arthritis, ankylosing spondylitis, and hidradenitis suppurativa as well.

Advantages/disadvantages

There are currently 11 FDA approved biologics to treat moderate-to-severe plaque psoriasis which are divided into four classes: TNF-α inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23/39 inhibitors. The TNF-α inhibitors are etanercept, infliximab, adalimumab, and certolizumab; the IL-12/23 inhibitor is ustekinumab; the IL-17 inhibitors are secukinumab, ixekizumab, and brodalumab, and the IL-23/39 inhibitors are guselkumab, tildrakizumab, and risankizumab.

Although all the classes are efficacious in the treatment of psoriasis, the relative efficacy of the biologics varies. A 2019 meta-analysis assessed the efficacy and safety of the different IL-12/23, IL-17, and IL-23/39 inhibitors used to treat moderate-to-severe plaque psoriasis and ranked these treatments according to their surface under cumulant ranking curves (SUCRA). Ixekizumab ranked the highest in achieving PASI70 short-term (93.0%), and brodalumab ranked the highest in achieving PASI100 short-term (85.0%). Secukinumab ranked the highest in achieving static physician’s global assessment (sPGA) 0/1, IGA 0/1, or PGA 0/1 (98.1%).

Another meta-analysis analyzed the efficacy of various biologics during randomized control trials. Relative efficacy was assessed as the percentage of participants who achieved PASI90. Treatments were ranked from the most to least efficacious according to SUCRA: infliximab (risk ratio (RR) 50.19, 95% confidence interval (CI) 20.92 to 120.45), bimekizumab (RR 30.27, 95% CI 25.45 to 36.01), ixekizumab (RR 30.19, 95% CI 25.38 to 35.93), and risankizumab (RR 28.75, 95% CI 24.03 to 34.39). In addition, infliximab, all four IL-17 inhibitors, risankizumab, and guselkumab achieved a higher PASI90 than ustekinumab, etanercept, adalimumab, and certolizumab.

Both of these meta-analyses conclude that the IL-17 inhibitors are among the most efficacious biologics in treating psoriasis, which is a major advantage of this class. While there have not been many head-on-head trials comparing bimekizumab with other IL-17 inhibitors, one head-on-head trial comparing bimekizumab and secukinumab concluded that bimekizumab was more efficacious in treating psoriasis than secukinumab. The higher efficacy of bimekizumab may be due to bimekizumab’s inhibition of both IL-17A and IL-17F, as compared to secukinumab’s selective inhibition of IL-17A.

Generally, biologics are a relatively safe and tolerable option for the treatment of moderate-to-severe plaque psoriasis. More specifically, IL-17 inhibitors also have mild to moderate safety profiles which commonly consist of upper respiratory tract infections and nasopharyngitis. A disadvantage of IL-17 inhibitors, however, is the increased risk of developing mucocutaneous candidiasis, which may be due in part to the immune-protective role of the IL-17 pathway in preventing fungal infections. Another disadvantage of IL-17 inhibitors is they may exacerbate inflammatory bowel disease (IBD). Patients with a history of IBD should either be monitored closely or not be administered IL-17 inhibitors at all.

Discussion

Psoriasis is an inflammatory skin disease that is associated with several comorbidities, including cardiovascular, renal, gastrointestinal, and psychiatric diseases. Furthermore, uncontrolled moderate-to-severe plaque psoriasis can be an extremely debilitating disease as it affects a large BSA and can significantly decrease quality of life. Biologics offer an efficacious and safe systemic treatment option for moderate-to-severe plaque psoriasis. There are currently 11 FDA approved biologics that are divided into four classes: TNF-alpha inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23/39 inhibitors.

There are currently three IL-17 inhibitors approved to treat psoriasis, which target IL-17A or IL-17 receptor type A. If approved, bimekizumab would be the fourth IL-17 inhibitor to treat psoriasis, and because it uniquely underwent affinity maturation to selectively inhibit both IL-17A and IL-17F, this may potentially increase its therapeutic efficacy.
IL-17 inhibitors are important in the treatment of psoriasis as IL-17 is a major cytokine in the pathogenesis of psoriatic plaques. IL-17’s action in the pathogenesis of plaque psoriasis is multifaceted as it causes the release of several proteins that cause psoriasis, activates other proteins to drive plaque formation, and activates cytokines that cause epidermal hyperplasia.8

Bimekizumab has undergone several phase II and III studies and was more effective in treating moderate-to-severe plaque psoriasis than placebo as concluded in the phase II BE ABLE and phase III BE READY trial, ustekinumab in the phase III BE VIVID trial, adalimumab in the phase III BE SURE trial, and secukinumab in the phase III BE RADIANT trial. Bimekizumab has a benign safety profile, and the most common AEs were nasopharyngitis, upper respiratory tract infection, arthralgias, and oral candidiasis during clinical trials.11-15

Bimekizumab’s efficacy in treating moderate-to-severe plaque psoriasis and its safety profile make it potentially a valuable biologic. While there are already several biologics available, there are many patients who may be resistant to treatment or might develop resistance to treatment with these biologics. There is also always the potential for non-response to biologics or decreased response, secondary to immunogenicity. Thus, bimekizumab presents another potential therapeutic in the arsenal of biologics already approved for psoriasis.16

Disclosure statement

Feldman has received research, speaking and/or consulting support from Eli Lilly and Company, GlaxoSmithKline/Stiefel, AbbVie, Janssen, Alvotech, vTv Therapeutics, Bristol-Myers Squibb, Samsung, Pfizer, Boehringer Ingelheim, Amgen, Dermavant, Arcutis, Novartis, Novan, UCB, Helsinn, Sun Pharma, Almirall, Galderma, Leo Pharma, Mylan, Celgene, Ortho Dermatology, Menlo, Merck & Co, Quient, Forte, Arena, Biocon, Accordant, Argenx, Sanofi, Regeneron, the National Biological Corporation, Caremark, Teladoc, Eurofins, Informa, UpToDate and the National Psoriasis Foundation. He is founder and part owner of Causa Research and holds stock in Sensal Health. Koppu, Singh, and Kaur have no conflicts to disclose.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Author consent

All authors listed meet ICMJE authorship criteria.

References

1. Korman NJ. Management of psoriasis as a systemic disease: what is the evidence? Br J Dermatol. 2020 Apr;182(4):840–848. doi: 10.1111/bjd.18245. PMID: 31225638.
2. Singh R, Koppu S, Perche PO, Feldman SR. The cytokine mediated molecular pathophysiology of psoriasis and its clinical implications. Int J Mol Sci. 2021 Nov 26;22(23):12793. doi: 10.3390/ijms221212793. PMID: 34884596.
3. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. JAMA. 2020 May 19;323 (19):1945–1960. doi:10.1001/jama.2020.4006. PMID: 32427307.
4. Bellinati F, Gisondi P, Girolomoni G. Latest advances for the treatment of chronic plaque psoriasis with biologics and oral small molecules. Biologics. 2021 June 29;15:247–253. doi:10.2147/ BTT.S290309. PMID: 34329295.
5. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clin Med (Lond). 2021 May;21(3):170–173. doi:10.7861/clinmed.2021-0257. PMID: 34001566.
6. Monks G, Rivera-Oyola R, Lebwohl M. The psoriasis decision tree. J Clin Aesthet Dermatol. 2021 Apr;14(4):14–22. PMID: 34055182.
7. Ocampo DV, Gladman D. Psoriatic arthritis. F1000res. 2019 Sept 20;8:F1000 Faculty Rev-1665. PMID: 31583079. doi: 10.7573/dic.2021-4-1. PMID: 30181299.
8. Hawkes JE, Yan BY, Chan TC, Krueger JG. Discovery of the IL-23/ IL-17 signaling pathway and the treatment of psoriasis. J Immunol. 2018 Sept 15;201(6):1605–1613. doi:10.4049/jimmunol.1800013. PMID: 30218197.
9. Adams R, Maroof A, Baker T, Lawson ADG, Oliver R, Paveley R, Rapecki S, Shaw S, Vajjah P, West S, et al. Bimekizumab, a novel humanized IgG1 antibody that neutralizes both IL-17A and IL-17F. Front Immunol. 2020 Aug 21;11:1894. doi:10.3339/ fimmu.2020.01894. PMID: 32973785.
10. Reid C, Griffiths CEM. Psoriasis and treatment: past, present and future aspects. Acta Derm Venereol. 2020 Jan 30;100(3):200032. doi:10.2340/00015555-3386. PMID: 31971601.
11. Papp KA, Merola JF, Gottlieb AB, Griffiths CEM, Cross N, Peterson L, Cioffi C, Blauvelt A. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: results from BE ABLE 1, a 12-week randomized, double-blind, placebo-controlled phase 2b trial. J Am Acad Dermatol. 2018 Aug;79(2):277–286.e10. doi:10.1016/j.jaad.2018.03.037. PMID: 29609013.
12. Reich K, Papp KA, Blauvelt A, Langley RG, Armstrong A, Warren RB, Gordon KB, Merola JF, Okubo Y, Madden C, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. Lancet. 2021 Feb 6;397(10273):487–498. doi:10.1016/S0140-6736(21)00125-2. PMID: 33549193.
13. Gordon KB, Foley P, Krueger JG, Pinter A, Reich K, Vender R, Vanvoorden V, Madden C, White K, Cioffi C, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. Lancet. 2021 Feb 6;397(10273):475–486. doi:10.1016/S0140-6736(21)00126-4. PMID: 33549192.
14. Warren RB, Blauvelt A, Bagel J, Papp KA, Yamauchi P, Armstrong A, Langley RG, Vanvoorden V, De Cuyper D, Cioffi C, et al. Bimekizumab versus Adalimumab in plaque psoriasis. N Engl J Med. 2021 July 8;385(2):130–141. doi:10.1056/ NEJMoa2102388. PMID: 33891379.
15. Reich K, Warren RB, Lebwohl M, Gooderham M, Strober B, Langley RG, Paul C, De Cuyper D, Vanvoorden V, Madden C, et al. Bimekizumab versus Secukinumab in plaque psoriasis. N Engl J Med. 2021 July 8;385(2):142–152. doi:10.1056/ NEJMoa2102383. PMID: 33913800.
16. Godeau D, Petit A, Richard I, Roquelaure Y, Descatha A. Return-to-work, disabilities and occupational health in the age of COVID-19. Scand J Work Environ Health. 2021 July 1;47 (5):408–409. doi:10.5271/sjweh.3960. PMID: 34003294.
17. Bakar RS, Jaapar SJS, Azmi AF, Aun YC. Depression and anxiety among patients with psoriasis: a correlation with quality of life and associated factors. J Taibah Univ Med Sci. 2021 Mar 16;14(4):491–496. doi:10.1016/j.jtumed.2021.02.008. PMID: 34408605.
18. Freitas E, et al. Bimekizumab for the treatment of psoriasis. Drugs. 2021 Oct;81(15):1751–1762. doi:10.1007/s40265-021-01612-z. PMID: 34623614.
19. Freitas E, Torres T. Bimekizumab: the new drug in the biologics armamentarium for psoriasis. Drugs Context. 2021 June 8;10:2021- 4–1. doi:10.7573/djcontext.2021-4-1.PMID: 34178093.
20. Reis J, Vender R, Torres T. Bimekizumab: the first dual inhibitor of interleukin (IL)-17A and IL-17F for the treatment of psoriatic
21. Glatt S, Helmer E, Haier B, Strimenopoulou F, Price G, Vajjah P, Harari OA, Lambert J, Shaw S. First-in-human randomized study of bimekizumab, a humanized monoclonal antibody and selective dual inhibitor of IL-17A and IL-17F, in mild psoriasis. Br J Clin Pharmacol. 2017 May;83(5):991–1001. doi: 10.1111/bcp.13185. PMID: 27859546.

22. Bai F, Li GG, Liu Q, Niu X, Li R, Ma H. Short-term efficacy and safety of IL-17, IL-12/23, and IL-23 inhibitors Brodalumab, Secukinumab, Ixekizumab, Ustekinumab, Guselkumab, Tildrakizumab, and Risankizumab for the treatment of moderate to severe plaque psoriasis: a systematic review and network meta-analysis of randomized controlled trials. J Immunol Res. 2019 Sept 10;2019:2546161. doi: 10.1155/2019/2546161. PMID: 31583255.

23. Sbidian E, Chaimani A, Garcia-Doval I, Doney L, Dressler C, Hua C, Hughes C, Naldi L, Afach S, Le Cleach L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2022 May 23;5(5):CD011535. doi: 10.1002/14651858.CD011535.pub5. PMID: 35603936; PMCID: PMC9125768.

24. Huppler AR, Bishu S, Gaffen SL. Mucocutaneous candidiasis: the IL-17 pathway and implications for targeted immunotherapy. Arthritis Res Ther. 2012 July 23;14(4):217. doi: 10.1186/ar3893. PMID: 22838497.