SKIN

Clinical Management Recommendations

Evaluating the Efficacy and Safety of Bimekizumab for Plaque Psoriasis and Psoriatic Arthritis: An Expert Consensus Panel Report

Danny Zakria, MD, MBA[1], Lauren Miller, PA-C[2], T.J. Chao, MPAS, PA-C[3], Kirk Gautier, PA-C[4], Holly Glover, MSEd, MPAS, MBA, PA-C[5], Kristine Kucera, DHSc, MPAS, PA-C[6], Andrea Nguyen, DMSc, MPAS, PA-C[7], Leigh Ann Pansch, MSN, FNP-BC, DCNP[8], Rachel Printy, PA-C[9], Cynthia Trickett, MPAS, PA-C[10], Joleen Volz, DMSc, PA-C[11], Milaan Shah, MD[1], Joshua Burshtein, MD[1]

[1] Icahn School of Medicine at Mount Sinai, New York, NY
[2] Southern Skies Dermatology and Surgery, Birmingham, AL
[3] Atlanta North Dermatology, Atlanta, GA
[4] US Dermatology Partners, Tyler, TX
[5] Metroplex Dermatology, Arlington, TX
[6] Bare Dermatology, Dallas, TX
[7] First Orange County Dermatology, Irvine, CA
[8] DOCS Dermatology, Cincinnati, OH
[9] US Dermatology Partners, Denver, CO
[10] North Dallas Dermatology Associates, Dallas, TX
[11] US Dermatology Partners, Corsicana, TX

ABSTRACT

Background: While there are numerous effective therapies for psoriasis, there remains an unmet need as some patients still suffer from inadequate response with available medications. Bimekizumab is a first-in-class monoclonal antibody that inhibits both interleukin (IL)-17A and IL-17F and was recently approved by the Food and Drug Administration. The aim of this study was for a panel of experts in psoriasis management to review the available data on bimekizumab and create consensus statements on its use in clinical practice.
Methods: A comprehensive literature search of PubMed, Scopus, and Google Scholar was conducted for English-language original research articles, systematic reviews, and meta-analyses discussing the safety and efficacy of bimekizumab for moderate to severe plaque psoriasis and psoriatic arthritis. A panel of nine dermatology physician assistants and one dermatology nurse practitioner with significant expertise in the management of psoriasis convened virtually on December 16, 2023, to review the studies and create recommendations for their peers on the use of bimekizumab. A modified Delphi process was implemented to reach a consensus on these statements and the Strength of Recommendation Taxonomy was used to assign each one a strength of recommendation.
Results: The literature search resulted in 92 articles that met search criteria. After a thorough screening of these studies for relevance to the discussion questions, 20 articles remained and were distributed to each panelist prior to the meeting. The panel unanimously voted to

adopt 10 consensus recommendations and assigned all 10 statements a strength of recommendation of "A."
Conclusion: Bimekizumab has a very high efficacy in the treatment of moderate to severe psoriasis and psoriatic arthritis. It also has a favorable safety profile that is consistent with that of other biologics, except for an increased risk of oral candidiasis.

INTRODUCTION

Plaque psoriasis is a chronic, inflammatory skin condition that affects about 125 million adults and children worldwide.[1-3] In the United States, psoriasis is estimated to afflict 3.2% of adults, with approximately 80 new cases per 100,000 person-years.[2-4] In addition to the skin, the disease can involve the nails and joints and is associated with several comorbidities.[2] Psoriasis can have a significant negative impact on quality of life given its chronic relapsing-remitting course, associated symptoms, and stigma.[5-7] In recent years, several new treatments for psoriasis have become available, including both topical and systemic agents.[8] Commonly used systemic agents include biologics targeting tumor necrosis factor (TNF), interleukin (IL)-17, IL-12/23, and IL-23.[9]

Among these different targets, the IL-17 cytokines have been shown to be important mediators of psoriatic disease.[10,11] Most notably, IL-17A and IL-17F are frequently co-expressed and elevated in both psoriatic and non-psoriatic skin, serving as key drivers of psoriasis pathogenesis.[10,11] There are a few anti-IL-17 systemic therapies that have been approved by the Food and Drug Administration (FDA) for the treatment of moderate to severe plaque psoriasis. Ixekizumab and secukinumab both inhibit IL-17A while brodalumab inhibits IL-17RA.[12] Bimekizumab, recently approved by the FDA in October 2023, is the first monoclonal antibody that targets both IL-17A and IL-17F.[13,14] Despite its recent approval, there have been several phase 2 and phase 3 clinical trials with long-term data demonstrating the clinical efficacy and safety of bimekizumab.[15-29]

Given that some psoriasis patients still struggle to obtain or maintain adequate disease control despite the numerous treatments available, it is important to understand how a new medication can fit in to the therapeutic landscape. The purpose of this study was for a panel of experts in psoriasis management to review the literature and available data and provide consensus statements on the use of bimekizumab for plaque psoriasis and psoriatic arthritis (PsA).

METHODS

Literature Search and Study Selection

A comprehensive literature search of PubMed, Scopus, and Google Scholar was completed on December 1, 2023, using the keywords "psoriasis," "psoriatic arthritis," "bimekizumab," "efficacy," and "safety" along with the Boolean term "AND" for English-language original research articles, systematic reviews, and meta-analyses without date restrictions. Articles were then screened for relevance to the treatment of moderate to severe psoriasis and PsA with bimekizumab. A few additional articles discussing other biologic therapies were included for reference. The studies that met inclusion criteria were distributed to the panelists. Each member of the panel reviewed the selected articles and assigned

them a level of evidence based on Strength of Recommendation Taxonomy (SORT) criteria.[30] These levels include **level 1** (good-quality patient-oriented evidence such as systematic reviews or meta-analyses of good quality cohort studies or a prospective cohort study with good follow-up), **level 2** (limited-quality patient-oriented evidence such as retrospective cohort studies or prospective cohort studies with poor follow-up), or **level 3** (other evidence such as consensus guidelines, usual practice, opinion, or disease-oriented evidence).[30]

Development of Consensus Statements

The panel consisted of nine dermatology physician assistants and one dermatology nurse practitioner with significant expertise in managing psoriasis. The panel convened on December 16, 2023, to review and discuss the included studies and create consensus statements and recommendations on the use of bimekizumab for psoriasis and PsA. The panel utilized a modified Delphi method in order to reach a consensus for each statement.[31] This process entails two-thirds supermajority approval through serial rounds of real-time voting and is a frequently utilized method to create expert recommendations in dermatology.[32-35]

RESULTS

Literature Search and Study Selection

The literature search resulted in 92 articles that met the search criteria. After a thorough screening process, 19 studies were selected as relevant to the research question and were distributed to the panelists prior to the discussion.

Levels of Evidence Designation

The panel assigned level 1 evidence to all 19 articles that were evaluated (**Table 1**).

Consensus Statements

The panel developed 10 consensus statements on the use of bimekizumab to treat moderate to severe plaque psoriasis and PsA. All 10 of the statements received a unanimous (10/10) vote for adoption. The SORT criteria were utilized to assign a strength of recommendation to each of the statements, all of which were given a strength of "A" (**Table 2**).

Statement 1: *Data suggests there is a benefit of targeting IL-17F in addition to IL-17A to treat psoriasis. (SORT Level A)*

Numerous studies have shown that the IL-17 family of cytokines are key drivers in the pathogenesis of psoriasis.[10-12] This family of cytokines includes IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F.[10] Although IL-17A is the most potent of these cytokines, there is a greater concentration of IL-17F in psoriasis lesions.[36] IL-17A and IL-17F are often co-expressed and stimulate similar patterns of genes, leading to skin inflammation. These two cytokines have the highest homology (55%), and while the other members of the IL-17 cytokine family form homodimers, IL-17A and IL-17F are unique in that they can form heterodimers.[11] In pre-clinical models, both IL-17A and IL-17F were shown to work with tumor necrosis factor (TNF) to stimulate the production of key proinflammatory cytokines that increase tissue inflammation.[37] Additionally, when compared with IL-17A blockade alone, dual neutralization of IL-17A and IL-17F led to decreased levels of expression of inflammation-linked genes and cytokines.[20,37]

Table 1. SORT criteria levels of evidence for articles reviewed prior to the meeting.

Article	Level of Evidence
Armstrong A, Fahrbach K, Leonardi C, et al. Efficacy of Bimekizumab and Other Biologics in Moderate to Severe Plaque Psoriasis: A Systematic Literature Review and a Network Meta-Analysis. Dermatol Ther (Heidelb). 2022;12(8):1777-1792. doi:10.1007/s13555-022-00760-8	1
Blauvelt A, Papp KA, Merola JF, et al. Bimekizumab for patients with moderate to severe plaque psoriasis: 60-week results from BE ABLE 2, a randomized, double-blinded, placebo-controlled, phase 2b extension study. J Am Acad Dermatol. 2020;83(5):1367-1374. doi:10.1016/j.jaad.2020.05.105	1
Blauvelt A, Armstrong A, Merola JF, et al. Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Analysis of Mental Health and Associated Disorders. SKIN J Cutan Med. 2023;7(6):s300. doi:10.25251/skin.7.supp.300	1
Glatt S, Helmer E, Haier B, et al. 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;83(5):991-1001. doi:10.1111/bcp.13185	1
Gordon KB, Foley P, Krueger JG, 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 [published correction appears in Lancet. 2021 Mar 27;397(10280):1182]. Lancet. 2021;397(10273):475-486.	1
Gordon KB, Langley RG, Warren RB, et al. Bimekizumab Safety in Patients With Moderate to Severe Plaque Psoriasis: Pooled Results From Phase 2 and Phase 3 Randomized Clinical Trials. JAMA Dermatol. 2022;158(7):735-744. doi:10.1001/jamadermatol.2022.1185	1
Gordon KB, Langley RG, Warren RB, et al. Bimekizumab safety in patients with moderate to severe plaque psoriasis: Pooled data from up to three years of treatment in randomized phase 3 trials. Br J Dermatol. Published online November 10, 2023. doi:10.1093/bjd/ljad429	1
Kokolakis G, Warren RB, Strober B, et al. Bimekizumab efficacy and safety in patients with moderate-to-severe plaque psoriasis who switched from adalimumab, ustekinumab or secukinumab: results from phase III/IIIb trials. Br J Dermatol. 2023;188(3):330-340. doi:10.1093/bjd/ljac089	1
McInnes IB, Asahina A, Coates LC, et al. Bimekizumab in patients with psoriatic arthritis, naive to biologic treatment: a randomised, double-blind, placebo-controlled, phase 3 trial (BE OPTIMAL). Lancet. 2023;401(10370):25-37. doi:10.1016/S0140-6736(22)02302-9	1
Merola JF, Landewé R, McInnes IB, et al. Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: a randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE). Lancet. 2023;401(10370):38-48. doi:10.1016/S0140-6736(22)02303-0	1
Menter A, Gordon KB, Leonardi CL, Gu Y, Goldblum OM. Efficacy and safety of adalimumab across subgroups of patients with moderate to severe psoriasis. J Am Acad Dermatol. 2010;63(3):448-456. doi:10.1016/j.jaad.2009.09.040	1
Oliver R, Krueger JG, Glatt S, et al. Bimekizumab for the treatment of moderate-to-severe plaque psoriasis: efficacy, safety, pharmacokinetics, pharmacodynamics and transcriptomics from a phase IIa, randomized, double-blind multicentre study. Br J Dermatol. 2022;186(4):652-663. doi:10.1111/bjd.20827	1
Papp KA, Merola JF, Gottlieb AB, et al. 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-blinded, placebo-controlled phase 2b trial. J Am Acad Dermatol. 2018;79(2):277-286.e10. doi:10.1016/j.jaad.2018.03.037	1
Reich K, Papp KA, Blauvelt A, 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;397(10273):487-498. doi:10.1016/S0140-6736(21)00125-2	1
Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus Secukinumab in Plaque Psoriasis. N Engl J Med. 2021;385(2):142-152. doi:10.1056/NEJMoa2102383	1
Strober B, Paul C, Blauvelt A, et al. Bimekizumab efficacy and safety in patients with moderate to severe plaque psoriasis: two-year interim results from the open-label extension of the randomized BE	1

RADIANT phase 3b trial [published online ahead of print, 2023 May 12]. J Am Acad Dermatol. 2023;S0190-9622(23)00782-X.	
Strober B, Tada Y, Mrowietz U, et al. Bimekizumab maintenance of response through 3 years in patients with moderate-to-severe plaque psoriasis: results from the BE BRIGHT open-label extension trial. Br J Dermatol. 2023;188(6):749-759. doi:10.1093/bjd/ljad035	1
Thaci D, Vender R, de Rie MA, et al. Safety and efficacy of bimekizumab through 2 years in patients with moderate-to-severe plaque psoriasis: longer-term results from the BE SURE randomized controlled trial and the open-label extension from the BE BRIGHT trial. Br J Dermatol. 2023;188(1):22-31. doi:10.1093/bjd/ljac021	1
Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus Adalimumab in Plaque Psoriasis. N Engl J Med. 2021;385(2):130-141. doi:10.1056/NEJMoa2102388	1

Table 2. Consensus statements and recommendations for the use of bimekizumab for moderate to severe plaque psoriasis and psoriatic arthritis.

Consensus Statement/Recommendation	Strength of Recommendation	Consensus Vote
Data suggests there is a benefit of targeting interleukin (IL)-17F in addition to IL-17A to treat psoriasis.	A	10/10
By targeting IL-17 A and F, bimekizumab provides high disease clearance in psoriasis, even for biologic experienced patients.	A	10/10
Based on head-to-head studies, bimekizumab is more effective at treating moderate to severe psoriasis than secukinumab, adalimumab, and ustekinumab.	A	10/10
Based on head-to-head studies, bimekizumab works more quickly than secukinumab, adalimumab, ustekinumab for psoriasis.	A	10/10
Standard dosing for bimekizumab for psoriasis is convenient, with less frequent injections than other medications in the IL-17 class. The optimal dosage is 320mg every 4 weeks for 16 weeks, then every 8 weeks thereafter. For select patients, such as those >120 kg, continued dosing of 320 mg every 4 weeks after week 16 can be considered.	A	10/10
In head-to-head studies, bimekizumab's safety profile is similar to that of other biologics for psoriasis, with the exception of an increased incidence of oropharyngeal candidiasis. Most cases of oropharyngeal candidiasis were mild to moderate, easily managed, and did not result in discontinuation.	A	10/10
Bimekizumab is effective for the treatment of psoriatic arthritis across all five disease domains; including axial, peripheral, enthesitis, dactylitis, and skin/nail disease.	A	10/10

The prevalence of inflammatory bowel disease (IBD) is increased in patients with psoriasis. Despite targeting IL-17A and IL-17F, the incidence of IBD in patients treated with bimekizumab is not higher than the incidence seen with use of other IL-17 blockers; however, patients with active Crohn's disease or ulcerative colitis were excluded from the clinical trials.	A	10/10
Compared to traditional oral systemic therapies like methotrexate, cyclosporine, and acitretin for plaque psoriasis, biologic agents exhibit a favorable hepatic safety profile. Bimekizumab has a comparable hepatic safety profile to other currently FDA approved biologics for plaque psoriasis and there is no evidence to support more frequent monitoring of hepatic function tests in patients on bimekizumab compared to other biologics. Periodic monitoring is recommended at the provider's discretion.	A	10/10
The risk of suicidal ideation and behavior (SIB) with bimekizumab is rare and not greater than what is seen in the general psoriasis population. The data does not support an association of bimekizumab with SIB.	A	10/10

To date, bimekizumab is the first and only FDA-approved monoclonal antibody to target both IL-17A and IL-17F, and as a result has excellent efficacy in the treatment of psoriasis.[15,16,18-28] Additionally, in a head-to-head study with secukinumab, an anti-IL-17 biologic that only targets IL-17A[38], bimekizumab demonstrated superior efficacy.[22] One limitation of this study is that it is unclear if bimekizumab's superior efficacy is due to the dual blockade of both IL-17A and IL-17F or another factor, such as bimekizumab having higher affinity for the IL-17A cytokine. However, given the available data and the high prevalence of IL-17F in psoriatic skin[36], it is likely that there is a benefit to targeting both IL-17A and IL-17F.

Statement 2: *By targeting IL17 A and F, bimekizumab provides high disease clearance in psoriasis, even for biologic experienced patients. (SORT Level A)*

There have been several phase 2 and phase 3 clinical trials demonstrating bimekizumab's efficacy in treating psoriasis. In a phase 2b trial, participants were randomized to receive bimekizumab every 4 weeks at doses of 64 mg, 160 mg, 160 mg with 320 mg loading dose, 480 mg, or placebo.[20] The study found a significant dose-dependent response for the primary endpoint of at least a 90% reduction from baseline in Psoriasis Area and Severity Index (PASI90) at week 12, with more patients achieving PASI90 in the bimekizumab groups (46.2%-79.1%) than patients in the placebo arm (0%; p<0.0001 all doses).[20] Additionally, a greater number of bimekizumab-treated patients achieved PASI100 than placebo-treated patients (27.9%-60% vs 0%; p≤0.0002 all doses).[20] Furthermore, in a 60-week extension of this study, patients who initially achieved PASI90 and PASI100 maintained high levels of disease clearance through week 60 (PASI90: 80% to 100%; PASI100: 69% to 83%).[15]

In the pivotal phase 3 trial, 435 patients were randomized 4:1 to receive either bimekizumab 320 mg every 4 weeks (n=349) or placebo every 4 weeks (n=86).[16] At week 16, 91% of patients in the bimekizumab group achieved PASI90 compared to 1% in the placebo group (p<0.0001) and 93% of bimekizumab-treated patients achieved an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) compared to 1% of placebo-treated patients (p<0.0001).[16] Regarding secondary end points, PASI100 was achieved by 68% (p<0.0001) and an IGA score of 0 was achieved by 70% (p<0.0001) of patients taking bimekizumab.[16] Notably, disease clearance was durable, with responses being maintained through week 56.[16]

Bimekizumab can also provide high disease clearance in patients who have tried and failed other biologic therapies. Many of the pivotal trials excluded patients who had experienced primary failure (no response within 12 weeks) with other IL-17 blockers or who had failed multiple biologics. However, a real-world study that recruited 237 patients at 19 sites in Italy included 103 (43.5%) biologic-experienced patients, and 44 (18.6%) of those participants had failed multiple biologics.[39] After 16 weeks of treatment, there were no statistically significant differences between the two groups, with 91.1% of patients in the biologic-naïve group achieving PASI90 compared to 87.9% of patients in the biologic-experienced group.[39]

Additionally, Kokolakis et al pooled results from three phase 3/3b trials in which patients were switched to bimekizumab from adalimumab[26] (at week 24), ustekinumab[21] (at week 52), or secukinumab[22] (at week 48).[18] The study found that most of the PASI90 nonresponders achieved PASI90 4 weeks after switching to bimekizumab from

adalimumab (67%), ustekinumab (79%), or secukinumab (53%).[18] After 48 weeks of receiving bimekizumab, 91%, 90%, and 79% of PASI90 nonresponders were able to achieve PASI90 after switching from adalimumab, ustekinumab, or secukinumab, respectively.[18] Even responders who did achieve PASI90 on one of these three drugs maintained a durable clinical response after switching to bimekizumab. Among the adalimumab, ustekinumab, and secukinumab PASI 90 responders, 96% (adalimumab/bimekizumab), 100% (ustekinumab/bimekizumab), and 95% (secukinumab/bimekizumab) maintained a PASI90 response 48 weeks after the switch to bimekizumab.[18]

Statement 3: *Based on head-to-head studies, bimekizumab is more effective at treating moderate to severe psoriasis than secukinumab, adalimumab, and ustekinumab. (SORT Level A)*

There have been head-to-head studies that have directly compared the efficacy of bimekizumab to other biologics for psoriasis, including secukinumab, adalimumab, and ustekinumab.[21,22,26] Secukinumab is a selective IL-17A inhibitor approved for moderate to severe psoriasis.[38] In a phase 3b trial, significantly more patients in the bimekizumab group achieved PASI100 than the secukinumab group at week 16 (61.7% vs. 48.9%, p<0.001) and week 48 (67% vs. 46.2%, p<0.001), respectively.[22] A secondary endpoint was PASI90 at week 16, which 85.5% of patients in the bimekizumab arm achieved compared to 74.3% of patients in the secukinumab arm.[22]

Another head-to-head trial compared the efficacy of bimekizumab and adalimumab. Adalimumab is a TNF inhibitor also approved in the treatment of moderate to severe psoriasis.[40] In the head-to-head study, 86.2% of patients receiving bimekizumab had a PASI90 response at week 16, compared to 47.2% of patients receiving adalimumab (p<0.0001).[26] Furthermore, 85.3% of patients in the bimekizumab group achieved an IGA of 0 or 1 at week 16, compared to 57.2% of patients in the adalimumab group.[26]

Ustekinumab is an IL-12/23 inhibitor approved for moderate to severe psoriasis.[41] In a head-to-head trial, 85% of participants receiving bimekizumab had a PASI90 response versus 50% of participants receiving ustekinumab (p<0.0001) at week 16.[21] Similarly, at week 16, 84% of patients in the bimekizumab arm had an IGA response (defined as clear or almost clear skin with at least a two-point improvement from baseline) compared to 53% in the ustekinumab arm (p<0.0001).[21]

These results demonstrate that the efficacy of bimekizumab is both non-inferior and superior to that of secukinumab, adalimumab, and ustekinumab in the treatment of moderate to severe plaque psoriasis. Although there are no head-to-head studies with bimekizumab and the numerous other biologics, such as brodalumab (IL-17 receptor blocker), ixekizumab (IL-17A inhibitor), or the IL-23 inhibitors, a network meta-analysis (NMA) demonstrated that bimekizumab has statistical superiority over all other biologics in achieving PASI90 and PASI100 at 10-16 weeks.[42] Of note, since this NMA only compared efficacy results over a 10-16 week period, conclusions on long-term superiority are not as evident.

Statement 4: *Based on head-to-head studies, bimekizumab works more quickly than secukinumab, adalimumab, and ustekinumab for psoriasis. (SORT Level A)*

The speed in which a biologic elicits a response can be just as important as efficacy since many patients experience a major negative impact on quality of life because of their disease. Bimekizumab has consistently demonstrated a quick onset, despite not requiring a loading dose. In a phase 1 study, a mean reduction of at least 80% from baseline lesion severity score (LSS) and PASI65 were seen in the top two treatment groups at week 2.[14] In one of the phase 3 trials, 76% of patients receiving bimekizumab achieved PASI75 after only 4 weeks (one dose) of treatment compared to 1% of patients in the placebo group ($p<0.0001$).[16]

The head-to-head trials previously discussed also directly compare bimekizumab's speed of onset with the other biologic therapies. At week 4, 71% of participants receiving bimekizumab achieved PASI75 compared to 47.3% of participants receiving secukinumab ($p<0.001$).[22] In the head-to-head with adalimumab, 76.5% of patients in the bimekizumab group achieved PASI75 at week 4 compared to 31.4% in the adalimumab group ($p<0.001$).[26] Similarly, in the comparator trial with ustekinumab, 77% of patients receiving bimekizumab reached PASI75 compared to 15% receiving ustekinumab ($p<0.0001$).[21] These trials consistently demonstrate bimekizumab's superior efficacy and speed of onset compared to the other three therapies.

Statement 5: *Standard dosing for bimekizumab for psoriasis is convenient, with less frequent injections than other medications in the IL-17 class. The optimal dosage is 320mg every 4 weeks for 16 weeks, then every 8 weeks thereafter. For select patients, such as those >120 kg, continued dosing of 320 mg every 4 weeks after week 16 can be considered. (SORT Level A)*

In a phase 2b trial of bimekizumab, several different dosages were investigated, including 64 mg, 160 mg, 160 mg with initial 320 mg loading dose, 320 mg, and 480 mg every 4 weeks.[20] The trial showed that a dose of 320 mg of bimekizumab of bimekizumab every 4 weeks (without a loading dose) led to the highest PASI75, PASI90, and IGA responses.[20] In one of the pivotal phase 3 clinical trials, patients who achieved PASI90 on bimekizumab 320 mg every 4 weeks at week 16 were re-allocated (1:1:1) to receive bimekizumab 320 mg every 4 weeks, every 8 weeks, or placebo for weeks 16-56.[16] More patients receiving the dose every 8 weeks achieved PASI90 (91.0 vs. 86.8%) and PASI100 (83.0% vs. 70.8%) compared to every 4 weeks.[16]

This ability to decrease the frequency of dosing (and the lack of a loading dose) makes bimekizumab's dosing convenient for both clinicians and patients, with fewer overall injections than other biologic therapies. However, for some patients, such as those weighing more than 120 kg, every 4 week dosing can be continued at the clinician's discretion.

Statement 6: *In head-to-head studies, bimekizumab's safety profile is similar to that of other biologics for psoriasis, with the exception of an increased incidence of oropharyngeal candidiasis. Most cases of oropharyngeal candidiasis were mild to moderate, easily managed, and did not result in discontinuation. (SORT Level A)*

Bimekizumab's safety profile has been evaluated in several clinical trials, including head-to-head studies and open label extensions. In each of the head-to-head studies, there was no difference in the overall rate of treatment related adverse events (TRAEs) between bimekizumab and secukinumab, adalimumab, or

ustekinumab.[21,22,26] The most common TRAEs after switching from these medications to bimekizumab were nasopharyngitis, oral candidiasis, upper respiratory tract infection, and urinary tract infection.[18] In each head-to-head trial the rates of oral candidiasis with bimekizumab were 19.3% versus 3% with secukinumab[22], 9.5% versus 0% with adalimumab[26], and 15% versus 1% with ustekinumab[21], respectively. However, more than 99% of the oral candidiasis infections were categorized as mild to moderate and only three total patients (0.2%) discontinued bimekizumab due to this adverse event.[17] The vast majority were successfully treated according to standard protocols, typically with nystatin and/or fluconazole, for a median of 12 days.[17]

When considering exposure-adjusted incidence rates (EAIRs), the EAIR of elevated liver enzymes did not increase in patients who switched to bimekizumab from adalimumab, ustekinumab, or secukinumab.[18] Additionally, EAIRs for serious adverse events including malignancies, IBD, major adverse cardiovascular events (MACE), and serious hypersensitivity reactions were low during the active-comparator treatment periods and remained low after switching to bimekizumab.[18]

Statement 7: *Bimekizumab is effective for the treatment of psoriatic arthritis across all five disease domains; including axial, peripheral, enthesitis, dactylitis, and skin/nail disease. (SORT Level A)*

A few clinical trials have also investigated the efficacy and safety of bimekizumab in the treatment of PsA. The first was a phase 2b dose-ranging trial that compared placebo to 4 different doses of bimekizumab dosed every 4 weeks, including 16 mg, 160 mg, 160 mg with a one-time 320 mg loading dose, and 320 mg. After 12 weeks of treatment, significantly more patients in the 16 mg bimekizumab and 160 mg bimekizumab groups achieved at least a 50% improvement in the American College of Rheumatology (ACR50) response criteria.[43] In one of the pivotal phase 3 trials, patients were randomized to bimekizumab 160 mg every 4 weeks, placebo every 2 weeks, or the reference group of adalimumab 40 mg every 2 weeks.[28] At week 16, significantly more patients in the bimekizumab group (44%) reached ACR50 compared to the placebo group (10%) with an odds ratio of 7.1 ($p<0.0001$; adalimumab 46%).[28]

While the participants in this trial had never received any disease-modifying antirheumatic drugs (DMARDs), another phase 3 trial included patients with a history of inadequate response or intolerance to treatment with one or two TNF-alpha inhibitors. At week 16, 43% of patients receiving bimekizumab achieved ACR50, compared to 7% of patients receiving placebo ($p<0.0001$).[29] These results highlight substantial positive ACR50 response rates in biologic experienced PsA patients treated with bimekizumab, even in those who had a history of inadequate response.

Bimekizumab has also demonstrated efficacy in specific PsA domains. Minimal disease activity (MDA) refers to a composite measure of multiple psoriatic arthritis domains including joint disease, skin disease, and enthesitis.[44] At week 16, MDA was achieved by a statistically significantly greater proportion of patient in the bimekizumab group compared to the placebo group.[29] Additionally, a greater number of patients with dactylitis at baseline achieved complete resolution with bimekizumab after 16 weeks compared to placebo.[29] Another study demonstrated that bimekizumab is able to elicit rapid improvement of axial

spondyloarthritis.[45] Finally, a network meta-analysis found that 67.4% of patients taking bimekizumab achieved complete resolution of their nail psoriasis.[46]

Statement 8: *The prevalence of inflammatory bowel disease (IBD) is increased in patients with psoriasis. Despite targeting IL-17A and IL-17F, the incidence of IBD in patients treated with bimekizumab is not higher than the incidence seen with use of other IL-17 blockers; however, patients with active Crohn's disease or ulcerative colitis were excluded from the clinical trials. (SORT Level A)*

Multiple studies have identified an increased prevalence of inflammatory bowel disease (IBD) in patients with psoriasis.[47,48] This can likely be explained by similarities in the pathogenesis of the two diseases.[47] However, IL-17 blockade may worsen symptoms of IBD and in most clinical trials for IL-17 inhibitors, including those for bimekizumab, patients with active IBD were excluded.[49] Pooled data from a total of eight randomized clinical trials with two years of study treatment found that the EAIR for IBD was 0.1 per 100 person-years, and this incidence did not increase with longer exposure to treatment.[17] Across these clinical studies, there were a total of four cases of new-onset IBD with three of these cases resulting in discontinuation of bimekizumab.[17] This incidence is comparable to that seen with other IL-17 inhibitors.[50-52] Specifically, a meta-analysis found the EAIR of IBD for both secukinumab and ixekizumab to be 0.23 per 100 person-years and pooled data from five clinical trials for brodalumab found its EAIR of IBD to be 0.2 per 100 person-years.[51,52] Although these rates are low, the panel recommends considering other biologic therapies for psoriasis first in patients with IBD.

Statement 9: *Compared to traditional oral systemic therapies like methotrexate, cyclosporine, and acitretin for plaque psoriasis, biologic agents exhibit a favorable hepatic safety profile. Bimekizumab has a comparable hepatic safety profile to other currently FDA approved biologics for plaque psoriasis and there is no evidence to support more frequent monitoring of hepatic function tests in patients on bimekizumab compared to other biologics. Periodic monitoring is recommended at the provider's discretion. (SORT Level A)*

Methotrexate, cyclosporine, and acitretin were some of the first systemic therapies used in the treatment of plaque psoriasis and are commonly used to this day.[53-55] These medications are known to have various severe adverse effects, including hepatotoxicity.[56-58] Hepatotoxicity from methotrexate can include transaminitis, fatty liver disease, fibrosis, and cirrhosis.[56] Acitretin and cyclosporine are both associated with elevated liver function tests (LFTs) and hepatitis.[57,58] Newer biologic agents used to treat psoriasis have demonstrated a more favorable hepatic profile than these medications. Specifically, a pooled analysis of bimekizumab safety across eight clinical trials revealed an EAIR for elevated LFTs of 3.6 (3.0-4.4) per 100 person-years.[17] In one phase 3 trial that investigated bimekizumab and adalimumab safety and efficacy, the EAIR of elevated LFTs after 24 weeks of treatment was 5.5 (1.5-14.1) per 100 person-years for bimekizumab and 15.8 (7.9-28.3) per 100 person-years for adalimumab.[25] In this trial, patients on adalimumab switched to bimekizumab, and over time the EAIRs in both groups decreased and was not cumulative. For the bimekizumab-only group, the EAIR at one year was 2.2 (0.3-8.0) per 100 person-years and at two years was 1.6 (0.2-5.9) per 100 person-years.[25] In the

adalimumab/bimekizumab group, the EAIR at one year was 6.9 (2.5-15.0) per 100 person-years and at two years was 6.1 (2.4-12.5) per 100 person-years.[25]

Similarly, bimekizumab demonstrated a comparable hepatic safety profile to secukinumab and ustekinumab in the respective head-to-head trials. In the study with secukinumab, the EAIR for elevated LFTs for bimekizumab was 1.6 (0.2-5.6) per 100 person-years compared to 5.9 (3.5-9.2) per 100 person-years for secukinumab.[18] The overall proportion of patients with elevated LFTs was 5.6% for bimekizumab and 5.1% for secukinumab.[22] In the ustekinumab comparator trial, the EAIR for elevated LFTs for bimekizumab was 1.7 (0-9.7) per 100 person-years compared to 2.6 (0.7-6.6) per 100 person-years for ustekinumab.[18] The total proportion of patients with hepatic adverse events was also similar between the two drugs (3% bimekizumab vs 3% ustekinumab).[21]

Importantly, psoriasis has known associations with several other conditions, including metabolic syndrome, obesity, and alcohol use disorder.[59,60] Each of these conditions can have profound negative impacts on liver health and function, meaning some psoriasis patients may have baseline elevations in LFTs.[59,60] The package insert for bimekizumab[61] states, “Test liver enzymes, alkaline phosphatase, and bilirubin at baseline, periodically during treatment with BIMZELX and according to routine patient management.” This is an important consideration as there currently are no consensus guidelines on the definition of “routine patient management.” For many comparable biologic therapies, clinicians recommend obtaining baseline hepatic function tests for all patients prior to initiating treatment and if the results are normal to then monitor at 6 month intervals or once within the first year, then none thereafter.[62,63] Additional studies are needed to clarify best practice for bimekizumab, but based on the available data the panelists suggest that a similar approach is acceptable and can be used at the clinician’s discretion.

Statement 10: *The risk of suicidal ideation and behavior (SIB) with bimekizumab is rare and not greater than what is seen in the general psoriasis population. The data does not support an association of bimekizumab with SIB. (SORT Level A)*

Several studies have shown that patients with psoriasis have an increased prevalence of depression, suicidal ideation and behavior (SIB), attempted suicides, and completed suicides compared to matched controls.[64-66] In fact, surveys of patients with psoriasis have reported that up to half have experienced feelings of profound helplessness and isolation due to the functional limitations and psychosocial impact of their disease.[67,68] The reported percentage of psoriasis patients with depressive symptoms has varied from 9% to 55%, likely due to the use of different assessment criteria and study populations.[69] The link between psoriasis and depression has frequently been attributed to the disease being highly stigmatized due to the visible nature of psoriatic lesions.[70] However, newer theories indicate that inflammatory cytokines in psoriasis can cause physiologic and biochemical changes in the central nervous system, leading to symptoms of depression.[71] This is supported by evidence that proinflammatory cytokines including IL-1 and IL-6 are elevated in both depression and psoriasis.[71] This may explain why one study found that 6.6% of patients with psoriasis attempted suicide at some point in their life compared to 0% of controls without psoriasis but with other skin conditions.[72]

Safety data from the numerous clinical trials studying bimekizumab have shown that the risk of SIB while taking the drug is very low. The overall EAIR for adjudicated SIB when pooled from eight clinical trials was 0.1 (0-0.3) per 100 person-years.[17] In the head-to-head clinical trials, the rates of SIB were 0.3% for bimekizumab vs. 0% for secukinumab[22], <1% for bimekizumab vs. 1% for ustekinumab[21], and 0% for bimekizumab vs 0% for adalimumab/bimekizumab.[26] Furthermore, patients who switched from secukinumab, adalimumab, or ustekinumab to bimekizumab had an EIAR of 0% for SIB through one year.[18] One study analyzed mean Patient Health Questionnaire (PHQ)-9 score for patients taking bimekizumab and found that they were lower with bimekizumab than placebo and similar to active comaprators.[73] It also found that with over 7,166 person-years of bimekizumab therapy, the rates of adjudicated SIB (0.13 per 100 person-years), suicidal behavior (0.06 per 100 person-years), and completed suicides (0.01 per 100 person-years) were similar to rates associated with other IL-17A inhibitors and IL-23 inhibitors psoriasis.[73] These data indicate that bimekizumab does not have a causal association with SIB and the risk of SIB is similar to other psoriasis biologics currently approved by the FDA.

CONCLUSION

Bimekizumab is the first monoclonal antibody to inhibit both IL-17A and IL-17F and has recently been approved by the FDA to treat moderate to severe plaque psoriasis. This panel reviewed the available data from numerous clinical trials and head-to-head studies and found that the data supports that bimekizumab has superior efficacy and faster response than several other biologics. Additionally, it has a favorable safety profile comparable to other biologics, except for an increased incidence of oral candidiasis. The majority of the oral candidiasis cases seen in the clinical trial development programs were mild or moderate, did not result in discontinuation of therapy, and were easily treated per standard medical management.

Conflict of Interest Disclosures:
DZ, **MS**, **JB,** and **JV** have no disclosures. **LM** is a speaker for Abbvie, BMS, Sanofi Regeneron, Dermavant, UCB, and Lilly and is a consultant for AbbVie, BMS, Sanofi-Regeneron, Dermavant, UCB, Lilly, Ferndale, Novartis, Janssen, Galderma, Amgen, and Arcutis. **TJC** is a speaker and consultant for AbbVie, Amgen, Arcutis, Beiersdorf, BMS, Dermavant, EPI Health, Ferndale Labs, Galderma, Incyte, Janssen, Eli-Lilly, Ortho Dermatologics, Regeneron, Sanofi-Genzyme, Sun Pharma and UCB Pharma. **KG** has served as a speaker/consultant for Eli Lilly, AbbVie, Arcutis, BMS, Verrica, and Ortho Dermatologics. **HG** has served as a consultant, speaker, investigator, or advisory board member of AbbVie, Almirall, Arcutis Biotherapeutics, BMS, Cassiopea SpA, Dermavant Sciences, Inc., Eli Lilly, Ferndale, Galderma, Incyte, ISDIN, LEO Pharma, Mayne Pharma, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Verrica. **KK** is a speaker and/or consultant for AbbVie, Amgen, Arcutis, Beiersdorf, Bristol Myers Squibb, Galderma, Janssen, Leo Pharma, Novartis, Pfizer, Sun Pharma, and UCB. **AN** has served as a speaker, investigator and/or consultant for AbbVie, Almirall, Amgen, Arcutis, ASLAN, Beiersdorf, Boehringer Ingehlheim, Bristol Meyers Squibb, Dermira, Dermavant, EPI, Galderma, Incyte, ISDIN, Janssen, Lilly, LEO, Mayne, Novan, Novartis Pharmaceuticals, Ortho Dermatologics, Pfizer, Regeneron Pharmaceuticals, Sanofi Genzyme, Sun Pharma, and UCB. **LAP** has served on the speaker bureau for AbbVie, Arcutis, BMS, Biersdorf, Dermavant, Galderma, Jansen, Eli Lilly, Novartis, Pfizer, Sanofi-Regeneron, and UCB and serves as a consultant for Leo. **RP** has served as a consultant in the past for Regeneron, UCB, Bristol Myers Squibb, Novartis, Arcutis and Castle Biosciences. **CT** has served on the speaker bureau for AbbVie, Arcutis, BMS, Janssen, Journey, Eli Lilly, Sanofi-Regeneron, Sun, and UCB and is on the advisory board for Dermavant and Galderma.

Funding: None

Corresponding Author:
Danny Zakria, MD, MBA
234 E 85th St, 5th Floor

New York, NY 10028
Email: Dzakria13@gmail.com

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. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(2):205-212. doi:10.1111/jdv.13854
3. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014;70(3):512-516. doi:10.1016/j.jaad.2013.11.013
4. Parisi R, Symmons DPM, Griffiths CEM, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013;133(2):377-385. doi:10.1038/jid.2012.339
5. Augustin M, Reich K, Blome C, Schäfer I, Laass A, Radtke MA. Nail psoriasis in Germany: epidemiology and burden of disease. Br J Dermatol. 2010;163(3):580-585. doi:10.1111/j.1365-2133.2010.09831.x
6. Schmid-Ott G, Künsebeck HW, Jäger B, et al. Significance of the stigmatization experience of psoriasis patients: a 1-year follow-up of the illness and its psychosocial consequences in men and women. Acta Derm Venereol. 2005;85(1):27-32. doi:10.1080/00015550410021583
7. Fortune DG, Richards HL, Griffiths CE, Main CJ. Psychological stress, distress and disability in patients with psoriasis: consensus and variation in the contribution of illness perceptions, coping and alexithymia. Br J Clin Psychol. 2002;41(Pt 2):157-174. doi:10.1348/014466502163949
8. Gisondi P, Del Giglio M, Girolomoni G. Treatment Approaches to Moderate to Severe Psoriasis. Int J Mol Sci. 2017;18(11):2427. doi:10.3390/ijms18112427
9. Sbidian E, Chaimani A, Garcia-Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Skin Group, ed. Cochrane Database Syst Rev. Published online December 22, 2017. doi:10.1002/14651858.CD011535.pub2
10. Blauvelt A, Chiricozzi A. The Immunologic Role of IL-17 in Psoriasis and Psoriatic Arthritis Pathogenesis. Clin Rev Allergy Immunol. 2018;55(3):379-390. doi:10.1007/s12016-018-8702-3
11. Brembilla NC, Senra L, Boehncke WH. The IL-17 Family of Cytokines in Psoriasis: IL-17A and Beyond. Front Immunol. 2018;9:1682. Published 2018 Aug 2. doi:10.3389/fimmu.2018.01682
12. Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. Lancet. 2021;397(10275):754-766. doi:10.1016/S0140-6736(21)00184-7
13. BIMZELX[®] Approved by the U.S. FDA for the Treatment of Adults with Moderate to Severe Plaque Psoriasis | UCB. www.ucb.com. https://www.ucb.com/stories-media/Press-Releases/article/BIMZELXR-Approved-by-the-US-FDA-for-the-Treatment-of-Adults-with-Moderate-to-Severe-Plaque-Psoriasis
14. Glatt S, Helmer E, Haier B, et al. 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;83(5):991-1001. doi:10.1111/bcp.13185
15. Blauvelt A, Papp KA, Merola JF, et al. Bimekizumab for patients with moderate to severe plaque psoriasis: 60-week results from BE ABLE 2, a randomized, double-blinded, placebo-controlled, phase 2b extension study. J Am Acad Dermatol. 2020;83(5):1367-1374. doi:10.1016/j.jaad.2020.05.105
16. Gordon KB, Foley P, Krueger JG, 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;397(10273):475-486. doi:10.1016/S0140-6736(21)00126-4
17. Gordon KB, Langley RG, Warren RB, et al. Bimekizumab Safety in Patients With Moderate to Severe Plaque Psoriasis: Pooled Results From Phase 2 and Phase 3 Randomized Clinical Trials. JAMA Dermatol. 2022;158(7):735-744. doi:10.1001/jamadermatol.2022.1185
18. Kokolakis G, Warren RB, Strober B, et al. Bimekizumab efficacy and safety in patients with moderate-to-severe plaque psoriasis who switched from adalimumab, ustekinumab or secukinumab: results from phase III/IIIb trials. Br J Dermatol. 2023;188(3):330-340. doi:10.1093/bjd/ljac089
19. Oliver R, Krueger JG, Glatt S, et al. Bimekizumab for the treatment of moderate-to-severe plaque psoriasis: efficacy, safety, pharmacokinetics, pharmacodynamics and transcriptomics from a phase IIa, randomized, double-blind multicentre study. Br J Dermatol. 2022;186(4):652-663. doi:10.1111/bjd.20827

20. Papp KA, Merola JF, Gottlieb AB, et al. 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-blinded, placebo-controlled phase 2b trial. J Am Acad Dermatol. 2018;79(2):277-286.e10. doi:10.1016/j.jaad.2018.03.037
21. Reich K, Papp KA, Blauvelt A, 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 [published correction appears in Lancet. 2021 Feb 20;397(10275):670]. Lancet. 2021;397(10273):487-498. doi:10.1016/S0140-6736(21)00125-2
22. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus Secukinumab in Plaque Psoriasis. N Engl J Med. 2021;385(2):142-152. doi:10.1056/NEJMoa2102383
23. Strober B, Tada Y, Mrowietz U, et al. Bimekizumab maintenance of response through 3 years in patients with moderate-to-severe plaque psoriasis: results from the BE BRIGHT open-label extension trial. Br J Dermatol. 2023;188(6):749-759. doi:10.1093/bjd/ljad035
24. Strober B, Paul C, Blauvelt A, et al. Bimekizumab efficacy and safety in patients with moderate to severe plaque psoriasis: Two-year interim results from the open-label extension of the randomized BE RADIANT phase 3b trial. J Am Acad Dermatol. 2023;89(3):486-495. doi:10.1016/j.jaad.2023.04.063
25. Thaçi D, Vender R, de Rie MA, et al. Safety and efficacy of bimekizumab through 2 years in patients with moderate-to-severe plaque psoriasis: longer-term results from the BE SURE randomized controlled trial and the open-label extension from the BE BRIGHT trial. Br J Dermatol. 2023;188(1):22-31. doi:10.1093/bjd/ljac021
26. Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus Adalimumab in Plaque Psoriasis. N Engl J Med. 2021;385(2):130-141. doi:10.1056/NEJMoa2102388
27. Gordon KB, Langley RG, Warren RB, et al. Bimekizumab safety in patients with moderate to severe plaque psoriasis: Pooled data from up to three years of treatment in randomized phase 3 trials. Br J Dermatol. Published online November 10, 2023. doi:10.1093/bjd/ljad429
28. McInnes IB, Asahina A, Coates LC, et al. Bimekizumab in patients with psoriatic arthritis, naive to biologic treatment: a randomised, double-blind, placebo-controlled, phase 3 trial (BE OPTIMAL). Lancet. 2023;401(10370):25-37. doi:10.1016/S0140-6736(22)02302-9
29. Merola JF, Landewé R, McInnes IB, et al. Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: a randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE). Lancet. 2023;401(10370):38-48. doi:10.1016/S0140-6736(22)02303-0
30. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004;69(3):548-556.
31. Hsu CC, Sandford B. The Delphi technique: making sense of consensus. Published online 1-8 2007.
32. Berman B, Ceilley R, Cockerell C, et al. Appropriate Use Criteria for the Integration of Diagnostic and Prognostic Gene Expression Profile Assays into the Management of Cutaneous Malignant Melanoma: An Expert Panel Consensus-Based Modified Delphi Process Assessment. SKIN J Cutan Med. 2019;3(5):291-306. doi:10.25251/skin.3.5.1
33. Zakria D, Brownstone N, Berman B, et al. Incorporating Prognostic Gene Expression Profile Assays into the Management of Cutaneous Melanoma: An Expert Consensus Panel. SKIN J Cutan Med. 2023;7(1):556-569. doi:10.25251/skin.7.1.1
34. Richard MA, Barnetche T, Rouzaud M, et al. Evidence-based recommendations on the role of dermatologists in the diagnosis and management of psoriatic arthritis: systematic review and expert opinion. J Eur Acad Dermatol Venereol. 2014;28:3-12. doi:10.1111/jdv.12560
35. Thiboutot DM, Dréno B, Abanmi A, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol. 2018;78(2):S1-S23.e1. doi:10.1016/j.jaad.2017.09.078
36. Cole S, Manghera A, Burns L, et al. Differential regulation of IL-17A and IL-17F via STAT5 contributes to psoriatic disease. J Allergy Clin Immunol. Published online May 2023:S0091674923006644. doi:10.1016/j.jaci.2023.03.035
37. Iznardo H, Puig L. Dual inhibition of IL-17A and IL-17F in psoriatic disease. Ther Adv Chronic Dis. 2021;12:20406223211037846. Published 2021 Aug 12. doi:10.1177/20406223211037846
38. 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
39. Gargiulo L, Narcisi A, Ibba L, et al. Effectiveness and safety of bimekizumab for the treatment of plaque psoriasis: a real-life multicenter study-IL PSO (Italian landscape psoriasis). Front Med (Lausanne). 2023;10:1243843. Published 2023 Aug 8. doi:10.3389/fmed.2023.1243843
40. Menter A, Gordon KB, Leonardi CL, Gu Y, Goldblum OM. Efficacy and safety of adalimumab across subgroups of patients with moderate to severe psoriasis. J Am Acad Dermatol. 2010;63(3):448-456. doi:10.1016/j.jaad.2009.09.040
41. 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) [published correction appears in Lancet. 2008 May 31;371(9627):1838]. Lancet. 2008;371(9625):1665-1674. doi:10.1016/S0140-6736(08)60725-4
42. Armstrong A, Fahrbach K, Leonardi C, et al. Efficacy of Bimekizumab and Other Biologics in Moderate to Severe Plaque Psoriasis: A Systematic Literature Review and a Network Meta-Analysis. Dermatol Ther (Heidelb). 2022;12(8):1777-1792. doi:10.1007/s13555-022-00760-8
43. Ritchlin CT, Kavanaugh A, Merola JF, et al. Bimekizumab in patients with active psoriatic arthritis: results from a 48-week, randomised, double-blind, placebo-controlled, dose-ranging phase 2b trial. The Lancet. 2020;395(10222):427-440. doi:10.1016/S0140-6736(19)33161-7
44. Chew E, Perin J, Grader-Beck T, Orbai AM. Measurement of Minimal Disease Activity in Psoriatic Arthritis Using the Patient-Reported Outcomes Measurement Information System-Physical Function or the Health Assessment Questionnaire Disability Index. Arthritis Care Res (Hoboken). 2022;74(1):151-160. doi:10.1002/acr.24433
45. Van Der Heijde D, Deodhar A, Baraliakos X, et al. Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials. Ann Rheum Dis. Published online January 17, 2023:ard-2022-223595. doi:10.1136/ard-2022-223595
46. Egeberg A, Kristensen LE, Puig L, et al. Network meta-analyses comparing the efficacy of biologic treatments for achieving complete resolution of nail psoriasis at 24-28 and 48-52 weeks. J Dermatolog Treat. 2023;34(1):2263108. doi:10.1080/09546634.2023.2263108
47. Fu Y, Lee CH, Chi CC. Association of Psoriasis With Inflammatory Bowel Disease: A Systematic Review and Meta-analysis. JAMA Dermatol. 2018;154(12):1417-1423. doi:10.1001/jamadermatol.2018.3631
48. Li Y, Guo J, Cao Z, Wu J. Causal Association Between Inflammatory Bowel Disease and Psoriasis: A Two-Sample Bidirectional Mendelian Randomization Study. Front Immunol. 2022;13:916645. Published 2022 Jun 10. doi:10.3389/fimmu.2022.916645
49. Hueber W, Sands BE, Lewitzky S, et al. Secukinumab, a human anti-IL-17A monoclonal antibody, for moderate to severe Crohn's disease: unexpected results of a randomised, double-blind placebo-controlled trial. Gut. 2012;61(12):1693-1700. doi:10.1136/gutjnl-2011-301668
50. Blauvelt A, Gooderham M, Iversen L, et al. Efficacy and safety of ixekizumab for the treatment of moderate-to-severe plaque psoriasis: Results through 108 weeks of a randomized, controlled phase 3 clinical trial (UNCOVER-3) [published correction appears in J Am Acad Dermatol. 2019 Jan;80(1):301]. J Am Acad Dermatol. 2017;77(5):855-862. doi:10.1016/j.jaad.2017.06.153
51. Reich K, Thaçi D, Stingl G, et al. Safety of Brodalumab in Plaque Psoriasis: Integrated Pooled Data from Five Clinical Trials. Acta Derm Venereol. 2022;102:adv00683. doi:10.2340/actadv.v102.1993
52. Truong SL, Chin J, Liew DFL, et al. Systematic Review and Meta-Analysis of Inflammatory Bowel Disease Adverse Events with Anti-Interleukin 17A Agents and Tumor Necrosis Factor Inhibitors in Rheumatic Disease and Skin Psoriasis. Rheumatol Ther. 2021;8(4):1603-1616. doi:10.1007/s40744-021-00360-6
53. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. J Am Acad Dermatol. 2009;60(5):824-837. doi:10.1016/j.jaad.2008.11.906
54. Rosmarin DM, Lebwohl M, Elewski BE, Gottlieb AB; National Psoriasis Foundation. Cyclosporine and psoriasis: 2008 National Psoriasis Foundation Consensus Conference. J Am Acad Dermatol. 2010;62(5):838-853. doi:10.1016/j.jaad.2009.05.017
55. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020;82(6):1445-1486. doi:10.1016/j.jaad.2020.02.044

56. Zachariae H. Methotrexate side-effects. Br J Dermatol. 1990;122 Suppl 36:127-133. doi:10.1111/j.1365-2133.1990.tb02890.x
57. Silva FS, Ribeiro MP, Santos MS, Rocha-Pereira P, Santos-Silva A, Custódio JB. Acitretin affects bioenergetics of liver mitochondria and promotes mitochondrial permeability transition: potential mechanisms of hepatotoxicity. Toxicology. 2013;306:93-100. doi:10.1016/j.tox.2013.01.020
58. Patocka J, Nepovimova E, Kuca K, Wu W. Cyclosporine A: Chemistry and Toxicity - A Review. Curr Med Chem. 2021;28(20):3925-3934. doi:10.2174/0929867327666201006153202
59. Langan SM, Seminara NM, Shin DB, et al. Prevalence of Metabolic Syndrome in Patients with Psoriasis: A Population-Based Study in the United Kingdom. J Invest Dermatol. 2012;132(3):556-562. doi:10.1038/jid.2011.365
60. Svanström C, Lonne-Rahm SB, Nordlind K. Psoriasis and alcohol. Psoriasis Targets Ther. 2019;Volume 9:75-79. doi:10.2147/PTT.S164104
61. UCB, Inc. BIMZELX (bimekizumab-bkzx) [package insert]. US Food Drug Adm. Published online 2023. Accessed February 23, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761151s000lbl.pdf
62. Emer JJ, Frankel A, Zeichner JA. A practical approach to monitoring patients on biological agents for the treatment of psoriasis. J Clin Aesthetic Dermatol. 2010;3(8):20-26.
63. Ahn CS, Dothard EH, Garner ML, Feldman SR, Huang WW. To test or not to test? An updated evidence-based assessment of the value of screening and monitoring tests when using systemic biologic agents to treat psoriasis and psoriatic arthritis. J Am Acad Dermatol. 2015;73(3):420-428.e1. doi:10.1016/j.jaad.2015.06.004
64. Kurd S.K., Troxel A.B., Crits-Christoph P., Gelfand J.M. The risk of depression, anxiety, and suicidality in patients with psoriasis: A population-based cohort study. Arch. Dermatol. 2010;146:891–895. doi: 10.1001/archdermatol.2010.186
65. Dalgard F.J., Gieler U., Tomas-Aragones L., Lien L., Poot F.M., Jemec G.B.E., Misery L., Szabo C., Linder D., Sampogna F., et al. The psychological burden of skin diseases: A cross-sectional multicenter study among dermatological out-patients in 13 European countries. J. Investig. Dermatol. 2015;135:984–991. doi: 10.1038/jid.2014.530
66. Wu J.J., Feldman S.R., Koo J., Marangell L.B. Epidemiology of mental health comorbidity in psoriasis. J. Dermatol. Treat. 2018;29:487–495. doi: 10.1080/09546634.2017.1395800
67. Bewley A, Burrage DM, Ersser SJ, Hansen M, Ward C. Identifying individual psychosocial and adherence support needs in patients with psoriasis: a multinational two-stage qualitative and quantitative study. J Eur Acad Dermatol Venereol. 2014;28(6):763-770. doi:10.1111/jdv.12174
68. Ring L, Kettis-Lindblad A, Kjellgren KI, Kindell Y, Maroti M, Serup J. Living with skin diseases and topical treatment: patients' and providers' perspectives and priorities. J Dermatolog Treat. 2007;18(4):209-218. doi:10.1080/09546630701278224
69. Fabrazzo M, Romano F, Arrigo M, et al. A Multivariate Analysis of Depression Prevalence in Psoriasis Patients: A Cohort Study. Int J Environ Res Public Health. 2022;19(4):2060. Published 2022 Feb 12. doi:10.3390/ijerph19042060
70. Patel N, Nadkarni A, Cardwell LA, et al. Psoriasis, Depression, and Inflammatory Overlap: A Review. Am J Clin Dermatol. 2017;18(5):613-620. doi:10.1007/s40257-017-0279-8
71. Koo J, Marangell LB, Nakamura M, et al. Depression and suicidality in psoriasis: review of the literature including the cytokine theory of depression. J Eur Acad Dermatol Venereol. 2017;31(12):1999-2009. doi:10.1111/jdv.14460
72. Pompili M, Innamorati M, Trovarelli S, et al. Suicide risk and psychiatric comorbidity in patients with psoriasis. J Int Med Res. 2016;44(1 suppl):61-66. doi:10.1177/0300060515593253
73. Blauvelt A, Armstrong A, Merola JF, et al. Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Analysis of Mental Health and Associated Disorders. SKIN J Cutan Med. 2023;7(6):s300. doi:10.25251/skin.7.supp.300