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Onset of Plaque Psoriasis Treatment Responses With Anti–IL-17/IL-23 Biologic Therapies

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ABSTRACT

Background: The impact of psoriasis on quality of life arises from both physical symptoms, such as pain and pruritus, and the psychosocial effects of the often highly visible lesions. For patients with moderate-to-severe psoriasis seeking amelioration of these symptoms, time to onset of treatment response is an important consideration when determining an appropriate therapeutic approach with their healthcare provider.

Methods: In this review, we discuss the fluidity of the definition of rapid response and time-to-response expectations of patients with psoriasis receiving biologic therapies. Next, we focus on time to response of brodalumab, a human anti–interleukin-17 receptor A monoclonal antibody, in patients with moderate-to-severe psoriasis, as measured by the psoriasis area and severity index and the psoriasis symptom inventory. Brodalumab previously exhibited efficacy and safety in treatment of moderate-to-severe psoriasis in three phase 3 trials (AMAGINE-1/-2/-3), warranting further characterization of its ability to meet patient needs regarding rapidity of treatment response. Finally, we place time to response of brodalumab in the context of the current treatment landscape of biologic therapies for psoriasis (particularly those targeting the interleukin-17/interleukin-23 axis).

Results: Direct and indirect comparisons with other interleukin-targeting drugs support brodalumab's more rapid onset of treatment effects, including skin clearance and relief of itch and pain.

Conclusion: Brodalumab induces a rapid treatment response in patients with moderate-to-severe psoriasis and may promote earlier improvements in quality of life.

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INTRODUCTION

Psoriasis is a chronic inflammatory skin condition affecting 2% to 3% of the world's population.[1,2] The development of the characteristically pruritic plaques is driven by complex immune processes. Although topical therapies are among the first-line treatment options for mild psoriasis, many patients require phototherapy or systemic treatment, including oral and biologic drugs.[3] Treatment options differ not only in their mechanisms of action and side-effect profiles but also in the time needed to achieve treatment results. When evaluating differences in the time to treatment response, it is important to consider the profound effect that psoriasis can have on health and quality of life, as well as how that may shape patient expectations and preferences regarding response time.

Mental health comorbidities of psoriasis are well established. In patients with psoriasis, depressive symptoms may emerge from a combination of chronic physical pain and discomfort and the social stigma attached to the appearance of skin lesions.[4] Additionally, studies have suggested that the inflammatory milieu of psoriasis may be a causative link to depression.[5] In a 2008 survey, 63% of individuals with psoriasis reported significant self-consciousness, and more than one-third reported avoiding social activities because of their psoriasis.[6] For some patients, this psychosocial distress may occur alongside symptoms of clinical depression. For example, one large population analysis found that 28% of individuals with psoriasis experienced depressive symptoms and were 1.5 times more likely to have clinical depression compared with the general population.[7] In a study of >2000 patients with psoriasis, 62% experienced some symptoms of depression.[8] Although the etiology of depression in patients with psoriasis is complex, studies have shown statistically significant correlations between disease flares and

high levels of stress, as well as pruritus severity and depressive symptoms.[9,10] In a 2018 review, the prevalence of depression in patients with psoriasis (2.1% to 33.7%) was generally greater than that in patients without psoriasis (≤22.7%).[11] Furthermore, recent studies have shown increased odds of suicidal ideation and behavior in patients with psoriasis compared with patients without psoriasis (odds ratio range, 1.01 to 2.05).[11-13]

Given the effects that psoriasis can have on mental health and quality of life, the initiation of effective and rapidly acting treatment may confer multifaceted benefits.[14] In recent years, interleukin-17 (IL-17) has emerged as a promising target for biologic therapy. Brodalumab is a human monoclonal antibody that targets the IL-17 receptor A with high specificity; blockade of this receptor has been shown to inhibit the expression of multiple cytokines implicated in psoriasis pathogenesis.[15] Although previous studies have addressed efficacy and safety of brodalumab,[15,16] the rapidity of treatment response in the context of patient expectations and the current treatment landscape merits further examination.

Selecting the most appropriate treatment regimen requires balancing many concerns, including the need to rapidly ameliorate mental health comorbidities. However, it is challenging to assess this aspect of treatment because the definition of rapid onset varies. In this review, we assess patient expectations regarding time to response when initiating systemic biologic therapies and highlight various ways that rapid response has been defined. We then discuss evidence for the rapid treatment-effect onset of brodalumab, including improvement in symptoms of pain and pruritus. Finally, we consider time to response of brodalumab in indirect comparison with other biologics.

Patient Definitions of and Preferences for Rapid Response

The time to achieve clinically relevant treatment response is an important aspect of psoriasis management. However, the definition of rapid response to treatment varies, which can make it challenging to precisely capture patient preferences. In one discrete-choice experiment, 29.1% of patients with psoriasis considered a shorter time to moderate symptom improvement (defined as 50% improvement) as the most important factor in treatment, whereas 16.5% of patients considered a longer period of time between flares as the most important attribute.[17,18] Another discrete-choice experiment found that 13.0% of patients with psoriasis considered early onset of response (defined as psoriasis area and severity index 90% improvement [PASI 90] achieved 4 weeks after drug initiation) as the most important attribute of biologic therapy.[19] A 2020 systematic review of 25 studies on patient and physician preferences for psoriasis treatment found that rapid response was the most important attribute for patients in 2 studies.[20] However, measures of rapid response only accounted for 13.0% of efficacy measures, suggesting that additional studies on this aspect would further clarify the value that patients place on rapid response.

A 2019 analysis of an online survey of 500 adult patients in the United States with moderate-to-severe psoriasis (self-assessed as body surface area [BSA] involvement of ≥3%) more closely assessed patient preferences regarding rapid response. To participate in the survey, patients were required to have had prior systemic therapy (biologic or nonbiologic) within the last 12 months and must have expressed a desire for rapid treatment effect (defined as scoring ≥7 points on a 10-point scale in agreement with ≥1 of the following statements: "I want a medication that clears my skin more effectively" or "I miss out on aspects of my life because of psoriasis").[21]

In this analysis, when asked to rate the importance of rapid response (defined as a "rapid response where you can see that the medication is clearing skin quickly") on a scale of 1 (not at all important) to 10 (extremely important), most patients (≥90.0%) rated this as highly important (ie, ≥7 points). When specifically asked about expectations of onset of response of a hypothetical new systemic therapy, patients anticipated a 50% improvement in skin clearance in ~2 weeks (mean, 16.4 days) and complete skin clearance in ~4 weeks (mean, 33.8 days).[21]

Further analysis revealed that preferences varied among demographic subgroups regarding response expectations with the hypothetical systemic therapy (Table). For example, those

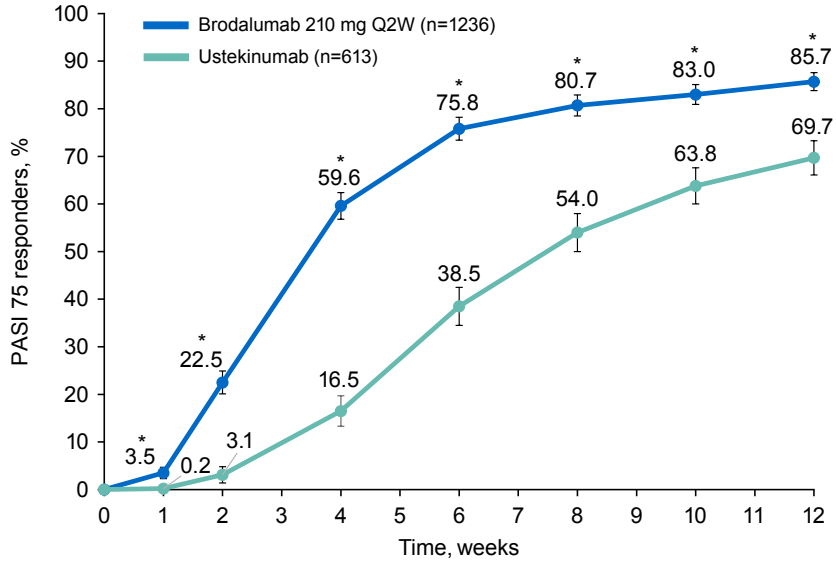
TABLE 1.

Patient Expectations for Achieving 50% Improvement With Hypothetical Systemic Therapy (N=500)[21,a]

Parameter	Number of days to 50% improvement
Sex	
Male	15.9
Female	16.8
Age, y	
18-30	14.8
31-40	15.3
41-50	16.6
51+	19.4
Disease severity[b]	
Moderate	15.5
Severe	18.5
Biologic experience	
Naive	18.6
Experienced	15.4

Bold parameters indicate subgroups with numerically fastest expectations for 50% improvement. [a]Participants must have expressed a desire for rapid treatment effect (defined as scoring ≥7 points on a 10-point scale in agreement with ≥1 of the following statements: "I want a medication that clears my skin more effectively" or "I miss out on aspects of my life because of psoriasis"). [b]Moderate and severe disease indicate body surface area involvement of 3% to 10% or >10%, respectively.

FIGURE 1. Percentage of patients achieving PASI 75 across 12 weeks (AMAGINE-2/-3).[22] Error bars represent 95% CI. Nonresponder imputed analysis. PASI 75, psoriasis area and severity index 75% improvement from baseline; Q2W, every 2 weeks. *P<0.001 vs ustekinumab starting from week 1.



with genital psoriasis expected 50% improvement by 13.3 days, whereas those with psoriasis in other difficult-to-treat areas, such as nails or scalp, expected longer time to 50% improvement (18.4 and 17.8 days, respectively). Patients who were younger, had moderate psoriasis, or had previous biologic therapy had a numerically stronger expectation of and assigned greater value to rapid therapeutic response compared with those who were older, had severe disease, or were naive to biologic therapy.[21]

Rapid Onset of Response in Patients Receiving Brodalumab

Skin Clearance

In two phase 3 studies (AMAGINE-2/-3), brodalumab 210 mg every 2 weeks (Q2W) was compared head-to-head with ustekinumab and demonstrated significantly faster onset of efficacy, as measured by PASI responses from baseline. Significant differences in speed of efficacy were observed early and persisted. As early as week 1, 3.5% and 0.2% of patients treated with brodalumab or ustekinumab, respectively, achieved PASI 75 (P<0.001). By week 12, 85.7% and 69.7% of patients treated with brodalumab or ustekinumab, respectively, achieved PASI 75 (P<0.001; Figure 1).[22]

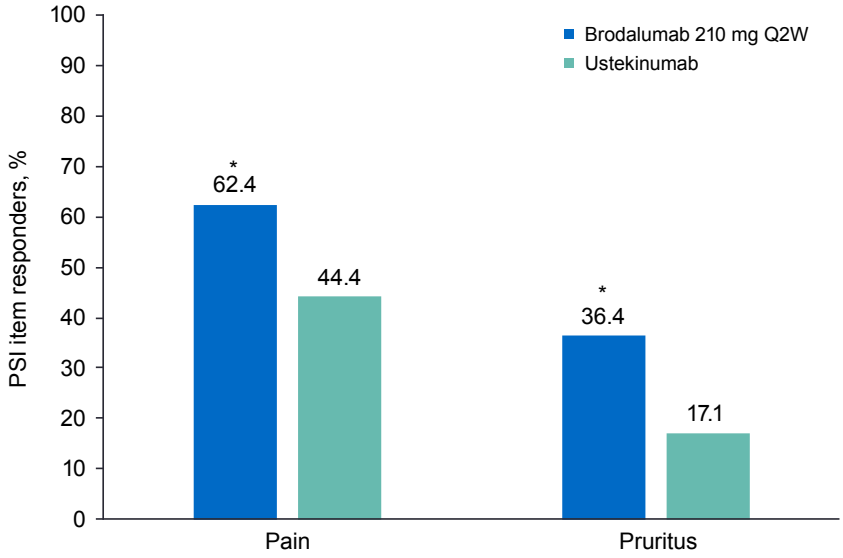
The median times to achieve all PASI landmarks (PASI 25, PASI 50, and PASI 75) were significantly shorter with brodalumab compared with ustekinumab (P<0.0001 for all analyses). The median times to achieve PASI 25, PASI 50, and PASI 75 were 0.8, 1.8, and 4.2 weeks, respectively, for patients receiving brodalumab, compared with 1.8, 4.5, and 9.4 weeks, respectively, for those receiving ustekinumab.[22] Furthermore, the estimated median times for 50% of patients to achieve PASI 75, PASI 90, or PASI 100 were significantly shorter with brodalumab (4.1, 6.4, and 12.4 weeks, respectively) compared with ustekinumab (8.1, 12.1, and median response for 50% of patients to achieve PASI 100 not reached during the study period, respectively).[23]

Symptoms

In addition to the appearance of psoriatic lesions, pain and pruritus are symptoms of psoriasis that frequently have a negative impact on quality of life. Rapid improvement of these symptoms is crucial to consider when selecting an appropriate therapeutic approach. Data from phase 3 studies of brodalumab have demonstrated rapid improvement in both pruritus and pain. Specifically, the psoriasis symptom inventory (PSI), an 8-item patient-reported outcome instrument designed to assess severity of psoriasis symptoms (including pruritus, redness, scaling, burning, stinging, cracking, flaking, and pain), has been used. Each symptom is scored from 0 (not at all severe) to 4 (very severe), with a total score ranging from 0 (best) to 32 (worst).[6]

In the integrated AMAGINE-1/-2/-3 studies, brodalumab 210 mg Q2W vs placebo was associated with a significantly greater proportion of overall PSI total score responders (defined as those who achieved PSI total score ≤8 and no item score >1) at week 2 (21.9% vs 2.1%; P<0.001). These improvements increased through week 12 compared with placebo. In AMAGINE-2/-3, brodalumab 210 mg Q2W vs ustekinumab was associated with a faster onset of symptom alleviation, with an estimated median time to PSI total score response (PSI ≤8) of 4 weeks. At week 12, brodalumab vs ustekinumab significantly increased the proportion of PSI responders who achieved a PSI total score of

FIGURE 2. Proportion of patients achieving improvement from baseline in PSI items of pain and pruritus at week 2 (AMAGINE-2/-3).[4,24] PSI, psoriasis symptom inventory; Q2W, every 2 weeks. *P<0.01 vs ustekinumab.



0 (22.7% vs 13.4%; P<0.001).[4] Notably, over the first 12 weeks in AMAGINE-1, brodalumab vs placebo was also associated with statistically significant improvements in anxiety and depression (measured by Hospital Anxiety and Depression Scale scores).[14]

In the integrated AMAGINE-1/-2/-3 studies, the PSI item score for pruritus significantly improved for patients receiving brodalumab 210 mg Q2W vs placebo as early as week 2 (36.1% vs 7.8%; P<0.001) and through week 12 (71.3% vs 13.2%; P<0.001). In AMAGINE-2/-3, brodalumab 210 mg Q2W vs ustekinumab induced rapid and sustained improvements in PSI item scores for pruritus and pain. Onset of significantly greater improvements began at week 2 for pruritus (36.4% vs 17.1%; P<0.01)[4] and week 2 for pain (62.4% vs 44.4%; P<0.01; Figure 2).[24] Significant treatment differences in response rates were observed with brodalumab vs ustekinumab through week 12 for pruritus (P<0.01) and through week 10 for pain (P<0.01).[24] Overall, brodalumab achieved rapid-onset milestones for the PSI total score, as well as for pain and pruritus scores, more quickly than comparators (placebo and ustekinumab).

Quality of Life

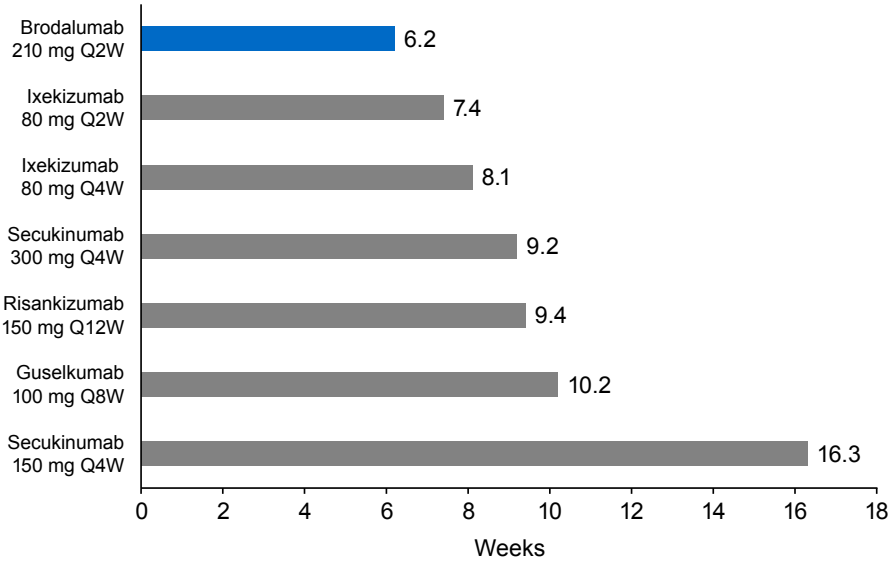
The dermatology life quality index (DLQI) is a 10-item, patient-reported measure of the social and psychologic impact of dermatologic disease. Total scores range from 0 to 30, with lower scores indicating a less severe impact on quality of life. In a secondary analysis of a phase 2 study, brodalumab (140 or 210 mg Q2W or 280 mg Q4W) vs placebo was associated with clinically meaningful improvements in DLQI (≥5.7-point reduction) as early as week 4 of treatment. At 12 weeks, DLQI scores were significantly improved in patients treated with brodalumab vs placebo.[6] Moreover, pooled analysis of phase 3 trials of brodalumab (AMAGINE-1/-2/-3) demonstrated that patients who achieved complete skin clearance with brodalumab (PASI 100) were more likely to have a DLQI score of 0 or 1 compared with those who almost achieved complete skin clearance (PASI 90 through PASI 100; 80.2% vs 62.7%, respectively).[7] These robust DLQI responses suggest that the time to response of brodalumab regarding physical signs of psoriasis may also correlate with timely achievement of quality-of-life improvement.

However, it is difficult to fully grasp the clinical implications of these DLQI data, as the approaches to measuring quality-of-life improvements vary across trials. For example, quality-of-life outcomes may be reported as achievement of a DLQI score of 0 or 1 vs a score of >1, as in a post hoc analysis of secukinumab, etanercept, and ustekinumab trials.[25] In AMAGINE-1, changes in DLQI were reported as the proportion of patients achieving a ≥5-point improvement from baseline to week 12 (brodalumab 210 mg, 83.6%; placebo, 21.6%), whereas in a trial of ixekizumab, changes were reported as the total change in DLQI score from baseline to week 12 (ixekizumab, -10.7; placebo, -2.6).[26,27] Although DLQI data for brodalumab are promising, more evidence is needed to determine the magnitude of effect compared with other IL-17 and IL-23 biologics.

An Indirect Comparison of the Onset of Response of Brodalumab and Other Biologics

In addition to studies directly comparing brodalumab with ustekinumab, time to response of brodalumab has been indirectly compared with that of other biologics. A 2020 meta-

FIGURE 3. Mean time for 50% of patients receiving IL-17 or IL-23 antagonists in clinical studies to achieve PASI 90. Loading doses (not shown) vary depending on biologic. Data for tildrakizumab were not available for this measure.[17] IL, interleukin; PASI 90, psoriasis area and severity index 90% improvement from baseline; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks.



analysis of IL-17 and IL-23 antagonists (brodalumab, guselkumab, ixekizumab, secukinumab, tildrakizumab, and risankizumab) showed that brodalumab 210 mg Q2W was associated with the most rapid onset of efficacy, as measured by the percentage of patients achieving improvements in PASI (data pooled from AMAGINE-1/-2/-3). The mean time for 50% of patients receiving brodalumab 210 mg Q2W to achieve PASI 75 was 3.5 weeks. Other biologics' onset for this measure ranged from 4.1 weeks (ixekizumab 160 mg loading dose, then 80 mg Q2W) to 9.3 weeks (tildrakizumab 100 or 200 mg at baseline and week 4, then Q12W).[17]

Brodalumab was also associated with the most rapid times to achieve PASI 90 and PASI 100 compared with other therapies. The mean time for 50% of patients receiving brodalumab 210 mg Q2W to achieve PASI 90 was 6.2 weeks (Figure 3). For other biologics, mean times for 50% of patients to achieve PASI 90 ranged from 7.4 weeks (ixekizumab 160 mg loading dose, then 80 mg Q2W) to 16.3 weeks (secukinumab 150 mg at baseline and weeks 1-4, then Q4W). The mean time for 25% of patients receiving brodalumab 210 mg Q2W to achieve PASI 100 was 6.9 weeks. For other biologics, mean times for 25% of patients to achieve PASI 100 ranged from 8.1 weeks (ixekizumab 160 mg loading dose, then 80 mg Q2W) to 15.1 weeks (secukinumab 150 mg at baseline and weeks 1-4, then Q4W).[17] Although the consensus on treatment outcomes is evolving, PASI 90 and PASI 100 are frequently used to assess psoriatic skin improvement and complete skin clearance, respectively.[7] Considering the value that patients place on not only efficacy but also rapidity of response, time to achievement of these PASI goals may indicate the ability of a biologic drug to meet patient expectations. The utility of PASI as a measurement of psoriasis improvement and the data here support the use of brodalumab to achieve rapid onset of clinically meaningful treatment response in patients with moderate-to-severe psoriasis.

DISCUSSION

Rapid onset is an important factor when considering patient preference for psoriasis therapy. Patient expectations regarding the rapidity of therapeutic response may vary by age, severity of disease, and prior experience with biologic drugs. However, the definition of rapid response can vary depending on subjective perceptions and standardized scoring tools. It is essential that clinicians understand each patient's preferences and expectations regarding time to onset of treatment effect so that these concerns can be balanced with other factors (eg, side effects).

Despite the complexity of defining rapid onset, data have shown that IL-17 inhibitors generally, and brodalumab specifically, achieve rapid onset of treatment milestones and ameliorate patient-reported signs and symptoms of moderate-to-severe plaque psoriasis. As measured by DLQI, patients who received brodalumab experienced clinically meaningful improvements in quality of life by week 4 of treatment. When compared with ustekinumab, brodalumab demonstrated both rapid onset of PASI response (estimated median time for 50% of patients to achieve PASI 90 was 6.4 vs 12.1 weeks, respectively) and higher proportions of improvements by week 2 in PSI item scores for pruritus (36.4% vs 17.1%; $P<0.01$) and pain (62.4 vs 44.4; $P<0.01$). Additional evidence from systemic analyses highlights the rapidity of response of brodalumab compared with other IL-17

and IL-23 inhibitors. However, because head-to-head studies have not been conducted, the statistical and clinical significance of these differences in outcomes, including onset of PASI response, are challenging to determine.

As additional biologics become available, assessing the relative effectiveness of treatment options is further complicated. Recently, results from clinical trials comparing the IL-17A and IL-17F inhibitor bimekizumab with placebo, adalimumab, and ustekinumab have been published.[28-30] In a pooled analysis of these trials, bimekizumab had a more rapid median time to PASI 90 response (8.0 weeks) vs adalimumab (12.6 weeks) and ustekinumab (12.6 weeks). Time to response of bimekizumab was also superior to adalimumab and ustekinumab when measured by PASI 100, investigator's global assessment of 0 or 1, and DLQI.[28] Although brodalumab had a median time to PASI 90 response of 6.2 weeks, bimekizumab and brodalumab have not been directly compared in a clinical study.

In three phase 3 clinical trials, brodalumab showed both efficacy and safety, as well as a rapid onset of therapeutic response, in patients with moderate-to-severe psoriasis. Given the well-established connection between psoriasis and psychosocial distress and depression, it is important to consider patient concerns regarding time to onset of response when recommending biologic therapy. Doing so will not only result in faster amelioration of physical symptoms such as pruritus and pain but may also allow for a more rapid improvement in overall quality of life. These data support brodalumab as a biologic option for patients with moderate-to-severe psoriasis seeking a rapid treatment response.

DISCLOSURES

Richard G. Fried is a consultant or serves on an advisory board for Almirall and Ortho Dermatologics (a division of Bausch Health US, LLC). Mark Lebwohl is an employee of Mount Sinai; receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics (a division of Bausch Health US, LLC), Regeneron, and UCB, Inc; and is a consultant for Aditum Bio, Almirall, AnaptysBio, Arcutis, Aristea, Arrive Technologies, Avotres Therapeutics, BioMx, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, LEO Pharma, Meiji, Mindera, Pfizer, and Verrica. Miriam Bettencourt is a consultant for AbbVie, Amgen, Ortho Dermatologics (a division of Bausch Health US, LLC), Pfizer, and Sun Pharma. John Koo is a speaker or advisor for AbbVie, Amgen, Dermavant, Janssen, Eli Lilly, EPI, LEO Pharma, Novartis, Ortho Dermatologics (a division of Bausch Health US, LLC), Pfizer, Regeneron/Sanofi, Sun Pharma, and UCB. Abby Jacobson is an employee of Ortho Dermatologics (a division of Bausch Health US, LLC).

REFERENCES

1. Stern RS, Nijsten T, Feldman SR, et al. Psoriasis is common, carries a substantial burden even when not extensive, and is associated with widespread treatment dissatisfaction. *J Investig Dermatol Symp Proc.* 2004;9(2):136-139.
2. Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. *J Am Acad Dermatol.* 2009;60(2):218-224.
3. Strober B, Sigurgeirsson B, Popp G, et al. Secukinumab improves patient-reported psoriasis symptoms of itching, pain, and scaling: results of two phase 3, randomized, placebo-controlled clinical trials. *Int J Dermatol.* 2016;55(4):401-407.
4. Gottlieb AB, Gordon K, Hsu S, et al. Improvement in itch and other psoriasis symptoms with brodalumab in phase 3 randomized controlled trials. *J Eur Acad Dermatol Venereol.* 2018;32(8):1305-1313.
5. Tohid H, Aleem D, Jackson C. Major depression and psoriasis: a psychodermatological phenomenon. *Skin Pharmacol Physiol.* 2016;29(4):220-230.
6. Gordon KB, Kimball AB, Chau D, et al. Impact of brodalumab treatment on psoriasis symptoms and health-related quality of life: use of a novel patient-reported outcome measure, the Psoriasis Symptom Inventory. *Br J Dermatol.* 2014;170(3):705-715.
7. Wu JJ. Contemporary management of moderate to severe plaque psoriasis. *Am J Manag Care.* 2017;23(21 Suppl):S403-S416.
8. Esposito M, Saraceno R, Giunta A, et al. An Italian study on psoriasis and depression. *Dermatology.* 2006;212(2):123-127.
9. Gupta MA, Gupta AK, Kirkby S, et al. A psychocutaneous profile of psoriasis patients who are stress reactors. A study of 127 patients. *Gen Hosp Psychiatry.* 1989;11(3):166-173.
10. Gupta MA, Gupta AK, Schork NJ, Ellis CN. Depression modulates pruritus perception: a study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria. *Psychosom Med.* 1994;56(1):36-40.
11. Wu JJ, Feldman SR, Koo J, Marangell LB. Epidemiology of mental health comorbidity in psoriasis. *J Dermatolog Treat.* 2018;29(5):487-495.
12. Singh S, Taylor C, Kornmehl H, Armstrong AW. Psoriasis and suicidality: a systematic review and meta-analysis. *J Am Acad Dermatol.* 2017;77(3):425-440.e2.
13. Koo J, Ho RS, Thibodeaux Q. Depression and suicidality in psoriasis and clinical studies of brodalumab: a narrative review. *Cutis.* 2019;104(6):361-365.
14. Thibodeaux Q, Fried R, Goldenberg G, et al. Expert panel discussion among psoriasis and psychodermatology specialists: how best to manage depressed psoriasis patients with brodalumab. *SKIN.* 2019;3(6):368-373. Available at: https://jofskin.org/index.php/skin/article/view/724. Accessed June 25, 2021.
15. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med.* 2015;373(14):1318-1328.
16. Papp K, Menter A, Leonardi C, et al. Long-term efficacy and safety of brodalumab in psoriasis through 120 weeks and after withdrawal and retreatment: subgroup analysis of a randomized phase III trial (AMAGINE-1). *Br J Dermatol.* 2020;183(6):1037-1048.
17. Egeberg A, Andersen YMF, Halling-Overgaard A-S, et al. Systematic review on rapidity of onset of action for interleukin-17 and interleukin-23 inhibitors for psoriasis. *J Eur Acad Dermatol Venereol.* 2020;34(1):39-46
18. Seston EM, Ashcroft DM, Griffiths CEM. Balancing the benefits and risks of drug treatment: a stated-preference, discrete choice experiment with patients with psoriasis. *Arch Dermatol.* 2007;143(9):1175-1179.
19. Tada Y, Ishii K, Kimura J, et al. Patient preference for biologic treatments of psoriasis in Japan. *J Dermatol.* 2019;46(6):466-477.
20. Sain N, Willems D, Charokopou M, Hiligsmann M. The importance of understanding patient and physician preferences for psoriasis treatment characteristics: a systematic review of discrete-choice experiments. *Curr Med Res Opin.* 2020;36(8):1257-1275.
21. Gorelick J, Shrom D, Sikand K, et al. Understanding treatment preferences in patients with moderate to severe plaque psoriasis in the USA: Results from a cross-sectional patient survey. *Dermatol Ther (Heidelb).* 2019;9(4):785-797.
22. Blauvelt A, Papp KA, Lebwohl MG, et al. Rapid onset of action in patients with moderate-to-severe psoriasis treated with brodalumab: a pooled analysis of data from two phase 3 randomized clinical trials (AMAGINE-2 and AMAGINE-3). *J Am Acad Dermatol.* 2017;77(2):372-374.

23. Blauvelt A, Lebwohl MG, Green LJ, et al. Median time to treatment response in patients with moderate-to-severe plaque psoriasis treated with brodalumab 210 mg or ustekinumab: a pooled analysis of data from two phase 3 randomized clinical trials (AMAGINE-2 and AMAGINE-3). Slides presented at: Annual Meeting of the American Academy of Dermatology; March 3-7, 2017; Orlando, FL.
24. Eichenfield LF, Armstrong A, Green L, et al. Improvements in lesional pain and itch symptoms with brodalumab in psoriasis studies. Poster presented at: Fall Clinical Dermatology Conference; October 12-15, 2017; Las Vegas, NV.
25. Hampton P, Halliday A, Aassi M, et al. Twelve-week secukinumab treatment is consistently efficacious for moderate-to-severe psoriasis regardless of prior biologic and non-biologic systemic treatment: post hoc analysis of six randomised trials. *J Eur Acad Dermatol Venereol.* 2021;35(4):928-937.
26. Strober B, Gordon K, Augustin M, et al. Improvements in patient-reported outcomes (PROs) among moderate to severe plaque psoriasis patients treated with brodalumab: results from AMAGINE-1. Slides presented at: Annual Meeting of the American Academy of Dermatology; March 4-8, 2016; Washington, DC.
27. Imafuku S, Torisu-Itakura H, Nishikawa A, et al, for the Japanese UNCOVER-1 Study Group. Efficacy and safety of ixekizumab treatment in Japanese patients with moderate-to-severe plaque psoriasis: subgroup analysis of a placebo-controlled, phase 3 study (UNCOVER-1). *J Dermatol.* 2017;44(11):1285-1290.
28. Lebwohl M, Hampton P, Morita A, et al. Speed of clinical response and improvement in psoriasis with bimekizumab: pooled results from the multicenter, randomized, double-blinded phase 3 BE VIVID, BE READY and BE SURE trials. Slides presented at: American Academy of Dermatology; April 23-25, 2021; Virtual.
29. 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.
30. 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.

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