A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

JDD

DRUGS • DEVICES • METHODS

Brodalumab: Five Years Of Real-World Safety And Efficiency

ISSN: 1545 9616

October 2023 • Volume 22 • Issue 10 (Supplement 1)

This supplement to the *Journal of Drugs in Dermatology* is funded by Ortho Dermatologics.

IS IT THE DISEASE OR THE DRUG?

Leon Kircik MD

Icahn School of Medicine at Mount Sinai, New York, NY
Physicians Skin Care, PLLC, Louisville, KY
DermResearch, PLLC, Louisville, KY
Skin Sciences, PLLC, Louisville, KY

The emergence of various biologic treatments in the field of dermatology has been termed the "Biologic Revolution", and for good reason. Two decades after the first biologic was approved for psoriasis, new biologics are now approved to treat atopic dermatitis, hidradenitis suppurativa, and other anticipated future indications. These treatments truly have changed how dermatologists treat inflammatory skin diseases like psoriasis and have substantially redefined patient expectations.

For the treatment of psoriasis, available biologic treatments target TNF, IL-23, or IL-17. All but one of the agents currently available binds to cytokines; brodalumab, a fully humanized IL-17 receptor A (IL-17RA) antagonist, binds to a cytokine receptor, making it unique among the biologics indicated for psoriasis.[1] When it comes to therapeutic formulations, sometimes the significance of a given distinction is unclear. In the case of brodalumab, cytokine receptor binding appears to affect clinical outcomes and differentiate its activity from that of other agents that target IL-17.

Head-to-head trials have not been conducted, but when looking at the phase 3 trial data for each of the IL-17 inhibitors individually, brodalumab appears to have the greatest efficacy by week 4 with respect to PASI75 response rates.[1-3] Brodalumab also leads in terms of Investigator Global Assessment (IGA) response at week 4, with rates between 83.3% to 84.6% (compared to 55.5%-59.2% and 43.1%-46.1%, respectively, for secukinumab and ixekizumab).[1-3]

Additionally, brodalumab demonstrates efficacy in a clinically meaningful, real-world treatment setting: retreatment capture rate. In studies for brodalumab, among patients who achieved PASI75 at week 12 and underwent withdrawal and retreatment, recapture rates were 100%, 96.9%, and 84.4% for PASI75, PASI90, and PASI100 responses, respectively, by week 24.[4-6]

Perhaps because it binds to the IL-17 cytokine receptor and not the cytokine directly, brodalumab also shows efficacy as a treatment option for patients who do not respond to other IL-17A inhibitors.[7,8] As well, it demonstrates efficacy for those with no or insufficient response to IL-12/23 inhibitors.[7] Data also suggest that brodalumab provides benefits for localized, difficult-to-treat areas of psoriasis, such as nail, scalp, or palmoplantar involvement.[9,10]

When multiple treatments emerge within a class, it may be challenging to ascertain their differences. In the case of brodalumab, evidence shows that this formulation has a distinct mechanism of action that appears to contribute to specific clinical utility. Plus, evidence shows that it is among the most cost-effective biologic treatment options for patients with moderate to severe psoriasis, an important practical consideration when starting patients on a biologic.[11]

However, we cannot ignore the warning of "suicidal ideation and behavior" in the package insert. Such warnings do not indicate drugs are not to be used. Rather, these warnings warrant our consideration and are intended to encourage thoughtful patient selection. Looking at the details of the suicide data from the studies always makes me wonder, "Is it the disease or the drug?"[12]

DISCLOSURE

Leon Kircik is compensated by *JDD* for his editorial support.

REFERENCES

1. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. *Br J Dermatol.* 2016;175(2):273-286.
2. 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.
3. Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. *N Engl J Med.* 2016;375(4):345-356.
4. Lebwohl M, Cather J, Armstrong A, et al. Recapture rate of brodalumab in patients with a lapse in treatment. *J Drugs Dermatol.* 2020;19(4):384-387.
5. Blauvelt A, Reich K, Warren RB, et al. Secukinumab re-initiation achieves regain of high response levels in patients who interrupt treatment for moderate to severe plaque psoriasis. *Br J Dermatol.* 2017;177(3):879-881.
6. Blauvelt A, Papp KA, Sofen H, et al. Continuous dosing versus interrupted therapy with ixekizumab: an integrated analysis of two phase 3 trials in psoriasis. *J Eur Acad Dermatol Venereol.* 2017;31(6):1004-1013.
7. Langley RG, Armstrong AW, Lebwohl MG, et al. Efficacy and safety of brodalumab in patients with psoriasis who had inadequate responses to ustekinumab: subgroup analysis of two randomized phase III trials. *Br J Dermatol.* 2019;180(2):306-314.
8. Kimmel G, Chima M, Kim HJ, et al. Brodalumab in the treatment of moderate to severe psoriasis in patients when previous anti-interleukin 17A therapies have failed. *J Am Acad Dermatol.* 2019;81(3):857-859.
9. Elewski B, Rich P, Lain E, et al. Efficacy of brodalumab in the treatment of scalp and nail psoriasis: results from three phase 3 trials. *J Dermatolog Treat.* 2022;33(1):261-265.
10. Nakagawa H, Niiro H, Ootaki K. Japanese brodalumab study group. Brodalumab, a human anti-interleukin-17-receptor antibody in the treatment of Japanese patients with moderate-to-severe plaque psoriasis: Efficacy and safety results from a phase II randomized controlled study. *J Dermatol Sci.* 2016;81(1):44-52.
11. Wu JJ, Feldman SR, Rastogi S, et al. Comparison of the cost-effectiveness of biologic drugs used for moderate-to-severe psoriasis treatment in the United States. *J Dermatolog Treat.* 2018;29(8):769-774.
12. Hashim PW, Chen T, Lebwohl MG, Marangell LB, Kircik LH. What Lies Beneath the Face Value of a BOX WARNING: A Deeper Look at Brodalumab. *J Drugs Dermatol.* 2018;17(8):s29-s34.

doi:10.36849/JDD.SF378632

ORIGINAL ARTICLE

Brodalumab is an Efficacious, Safe, and Cost-Effective IL-17 Receptor Blocker for the Treatment of Moderate-to-Severe Plaque Psoriasis: 2023 Update

Naiem T. Issa MD PhD,[a,b] Leon Kircik MD[c]

[a]Forefront Dermatology, Vienna, VA
[b]Issa Research & Consulting, LLC, Springfield, VA
[c]Icahn School of Medicine at Mount Sinai, New York, NY; Physicians Skin Care, PLLC Louisville, KY; DermResearch, PLLC Louisville, KY; Skin Sciences, PLLC Louisville, KY

ABSTRACT

Psoriasis remains a highly prevalent condition in the United States and worldwide. Preclinical research has been triumphant in elucidating the critical immunological pathways involved in psoriasis. There has been an evolution in biologics that paralleled the understanding of these pathways beginning with anti-tumor necrosis factor (TNF) inhibitors and now most recently the interleukin (IL)-23 and IL-17 axes. Numerous evidence-based studies demonstrate the efficacy of these agents for skin clearance in moderate-to-severe plaque psoriasis. Brodalumab, a fully humanized IL-17 receptor A (IL-17RA) antagonist, is wholly unique in that it binds to a cytokine receptor and not a cytokine itself unlike the other biologics indicated for psoriasis. This unique mechanism has lent an advantage where not only is brodalumab effective in treating moderate-to-severe plaque psoriasis, but it is also successful in psoriasis patients whose disease did not respond to other biologics. This review provides a summary of the efficacy of brodalumab in plaque psoriasis and difficult-to-treat locations (ie, scalp, nail, palmoplantar), in patients with psoriasis who failed to achieve minimum clearance with other biologics, and it illuminates the most recent pharmacovigilance data obtained from the past 5 years. Furthermore, the cost effectiveness of brodalumab is also discussed.

J Drugs Dermatol. 2023;22:10(Suppl 1):s5-14.

INTRODUCTION

Psoriasis is a significant health and economic burden. In the United States, the prevalence of psoriasis is estimated to be 7.4 million, which accounts for ~2.2% of the population, with the total economic burden estimated as $35.2 billion of which $11.2 billion is from productivity losses.[1] It is also associated with physical and emotional distress, thus leading to a significant reduction in the quality of life of those affected. Given the chronic nature of psoriasis and, therefore, the need for chronic therapy, long-term safe and effective therapeutics are critical.

As the pathophysiology of psoriasis has become well elucidated, a plethora of targeted treatments have emerged that inhibit different components of immunologic pathways implicated. Notably, interleukin (IL)-17 is thought to be a downstream effector, and its interaction with its receptor (IL-17R) is thought to be a critical signaling hub and a desirable target for inhibition.[2] Currently, there is only one inhibitor of IL-17RA – brodalumab.

Brodalumab is a fully human monoclonal antibody of specifically the IL-17RA subunit of the receptor complex.[3] It has been successful in achieving significant clearance as monotherapy in patients with moderate-to-severe plaque psoriasis. It also demonstrates efficacy in tough-to-treat areas such as the nails, scalp, palms, and soles.[4] Furthermore, recent studies have demonstrated additional utility in patients who have failed to achieve response with IL-17A inhibitors such as secukinumab and ixekizumab. Lastly, cost-effectiveness studies have determined brodalumab to be the most economical biologic for the treatment of moderate-to-severe plaque psoriasis in the United States.[5] This review will expand upon these details.

IL-17 Axis in Psoriasis

While numerous cytokines and chemokines have been implicated in the pathogenesis of psoriasis, the IL-23/IL-17 axis is a critical hub (Figure 1).[6,7] Interleukin-17 (IL-17) is a pro-inflammatory cytokine that is produced by a variety of immune cells, including T helper 17 (Th17) cells, gamma/delta T cells, and innate lymphoid cells. IL-17 promotes the recruitment and activation of immune cells in the skin, leading to the production of additional cytokines and chemokines, which contribute to the inflammation and tissue damage seen in psoriasis. Importantly, IL-23 plays a pivotal role in IL-17 secretion and acts upstream by inducing Th17 cells.[8]

IL-17 exerts its effects by binding to a receptor complex composed of IL-17RA and IL-17RC, which is expressed on a variety of cells, including keratinocytes, fibroblasts, and immune cells.[9] In addition, the IL-17 cytokine family consists of 6 isoforms (IL-17A-F), which may exert differential effects.[10] Upon binding to the receptor complex, IL-17 activates a signaling cascade that leads to the activation of transcription factors, such as nuclear factor kappa B (NF-κB) and activator protein 1 (AP-1). These transcription factors drive the expression of pro-inflammatory genes, such as IL-6, IL-8, and tumor necrosis factor alpha (TNF-α), which contribute to the development and maintenance of psoriatic lesions.

The importance of IL-17 in the pathogenesis of psoriasis is supported by several lines of evidence.[11] First, IL-17 is elevated in the serum and skin lesions of patients with psoriasis. Second, genetic studies have identified variants in genes related to the IL-17 pathway that are associated with an increased risk of psoriasis. Finally, therapies targeting the IL-17 pathway have shown significant efficacy in treating psoriasis.

Current Therapeutics Targeting IL-17 Axis

In the United States, there are 3 biologics currently approved for moderate-to-severe adult plaque psoriasis aimed at inhibiting the IL-17 pathway: secukinumab, ixekizumab, and brodalumab (Figure 1). Secukinumab and ixekizumab are fully human and humanized monoclonal antibodies, respectively, that inhibit the cytokine IL-17A,[12,13] Brodalumab is a fully human monoclonal antibody that blocks IL-17RA, thereby preventing all IL-17 isotypes (IL-17A-F) from interacting with their cognate receptors to block IL-17 signaling.[14]

IL-17 inhibitors have achieved rapid and substantial reductions in Psoriasis Area Severity Index (PASI) score, which takes into account the extent and severity of skin involvement, erythema (redness), induration (thickness), and desquamation (scaling) of psoriatic lesions. In the placebo-controlled phase 3 monotherapy trials of these inhibitors in adult moderate-to-severe plaque psoriasis, PASI75 response rates (ie, the proportion of patients achieving at least 75% reduction in PASI scores) at week 12 were comparable. PASI75 response rates range from 67% to 81% for secukinumab, 78% to 90% for ixekizumab, and 83% to 86% for brodalumab at week 12 in these trials.[14-17] PASI90 response rates at week 12 ranged from 54% to 59%, 49% to 71%, and 70% to 72%, respectively (Figure 2). For the most stringent endpoint, PASI100 (complete clearance), response rates at week 12 ranged from 24% to 35%, 29% to 44%, and 40% to 44%, respectively.

Long-term data from phase 3 trials have also shown sustained efficacy profiles. Secukinumab has shown sustained PASI75 response rates ranging from 73% to 83% at 52 weeks.[15] Similarly, ixekizumab has demonstrated PASI75 response rates of >80% at 52 weeks.[18] Brodalumab has also shown sustained efficacy, with PASI75 response rates of 69% to 85% at 52 weeks.[14,17] When comparing PASI75 response rates up to 5 years of treatment, results were also sustained. Secukinumab demonstrated a response rate of ~81%.[19] Ixekizumab demonstrated a greater response rate of 90%.[20] Brodalumab also demonstrated a similar response rate of over 80%.[21] These findings suggest that IL-17 inhibitors may provide durable and sustained efficacy in the treatment of psoriasis for up to at least 260 weeks of treatment.

Brodalumab Achieves Rapid Clearance Relative to IL-17A Inhibitors

As treatment for plaque psoriasis has become more sophisticated, so have the expectations for treatment goals. Patients are expecting long-term remission from psoriasis and a rapid time frame to achieve a clinically acceptable endpoint. While no head-to-head comparative studies have been conducted comparing biologics within the IL-17 family, brodalumab appears to have the greatest efficacy by week 4 concerning PASI75 response rates. In the phase 3 trials, response rates ranged from 38.1% to 86.3%, 57.4% to 82.1%, and 85.1% to 100% for secukinumab, ixekizumab, and brodalumab, respectively.[14-16] Investigator Global Assessment (IGA) response rates (achieving a score of clear [0] or almost clear [1] with ≥2 point improvement) at week 4 are as follows: 55.5% to 59.2%, 43.1% to 46.1%, and 83.3% to 84.6% for secukinumab, ixekizumab, and brodalumab, respectively. In performing an indirect comparison of time for 50% of patients receiving IL-17 or IL-23 antagonists to achieve PASI90, Fried et al found brodalumab to have the quickest mean time at 6.2 weeks, whereas ixekizumab and secukinumab both required greater than 7 weeks.[22]

Brodalumab Demonstrates High Levels of Recapture Response Among IL-17 Inhibitors

In real-world circumstances, patients may stop and restart treatment for a number of reasons such as cost, insurance barriers, inconveniences, psychological

FIGURE 1. IL-23/IL-17 axis in psoriasis. IL-23 stimulates Th17 cells to secrete IL-17, which exists as either a homodimer or heterodimer of 6 isoforms (IL-17A-F) of which 2 are shown (IL-17A/F). IL-17 binds to the IL-17 receptor complex, which is also a heterodimer of the IL-17RA and IL-17RC subunits, to elicit pro-inflammatory gene expression changes that further propagate the psoriasis disease state. Current approved biologics that specifically block the interaction of IL-17 with its receptor include secukinumab and ixekizumab, which directly inhibit the IL-17A cytokine, as well as brodalumab, which inhibits the IL-17RA subunit of the IL-17 receptor complex. Through the blocking of IL-17RA, all upstream IL-17 homodimers, and heterodimers are unable to bind and stimulate the IL-17 receptor complex.

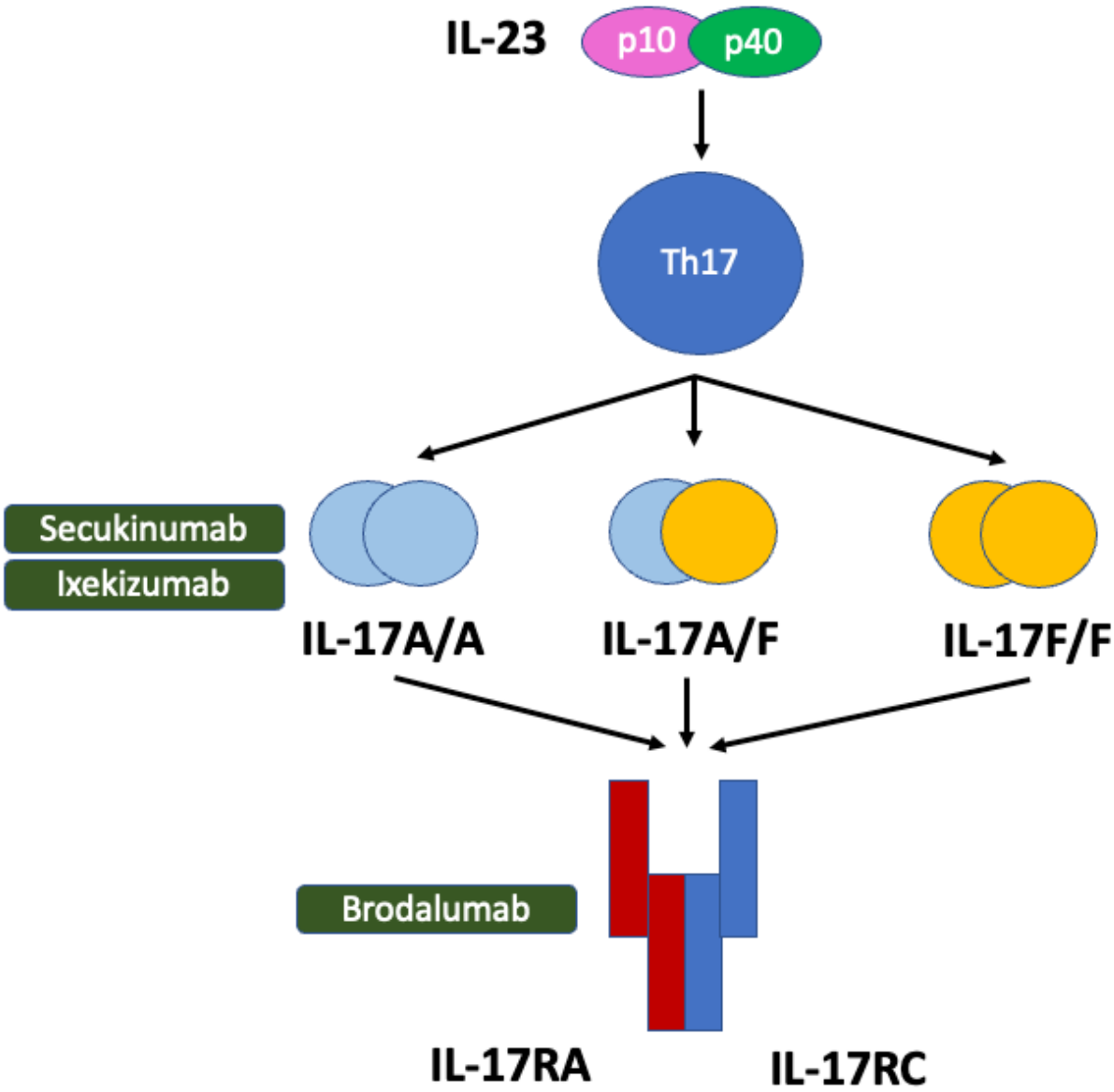
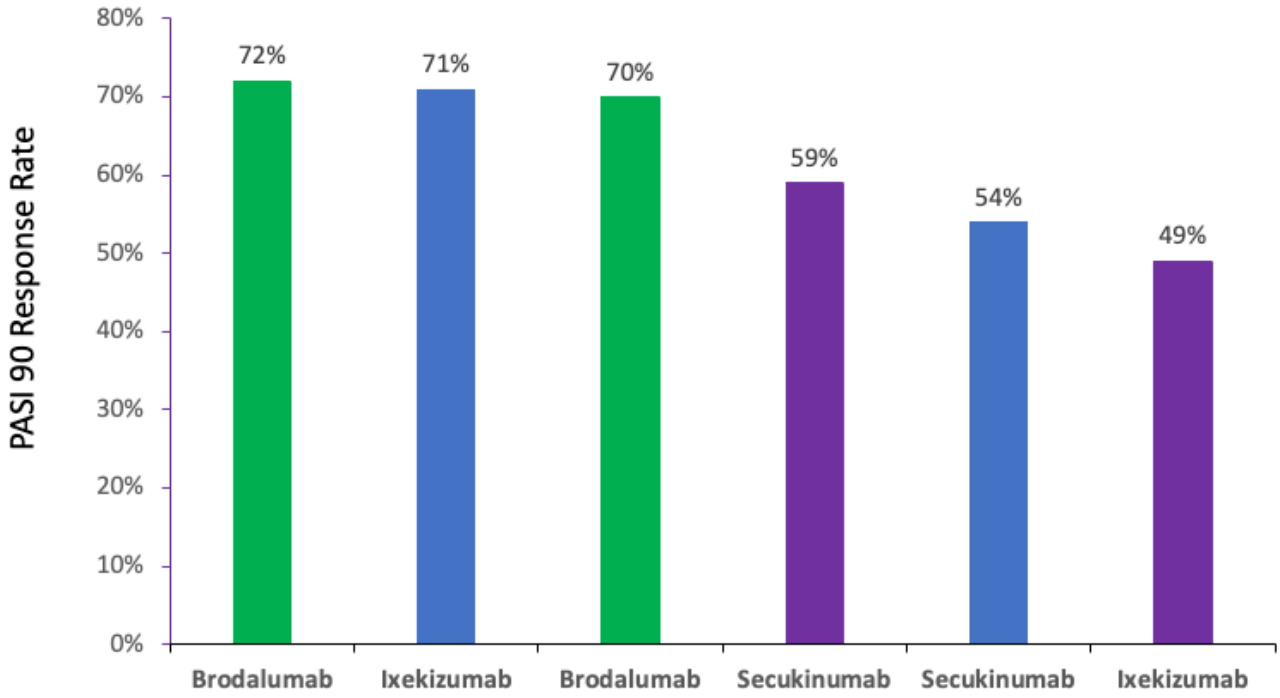


FIGURE 2. Waterfall plots of PASI 90 clearance rates for IL-17A and IL-17RA inhibitors after 12 weeks of treatment for moderate-to-severe psoriasis.



stress, and comorbidities, among others.[23] As such, it is important for treatment to recapture skin clearance after discontinuation and retreatment. The AMAGINE-1 phase 3 trial (NCT01708590) assessing the efficacy of brodalumab had a planned withdrawal phase at week 12 (patients were switched to placebo) with eligibility for retreatment starting at week 16 upon return of disease (defined as static physician's global assessment score [sPGA] of 3 or greater). Patients who achieved PASI75 at week 12 and underwent withdrawal and retreatment exhibited recapture rates of 100%, 96.9%, and 84.4% in PASI75, PASI90, and PASI100 responses, respectively by week 24.[24] Notably, recapture rates for PASI75 after withdrawal and retreatment for secukinumab and ixekizumab were 93.8% and 87.0%, respectively.[25,26]

Brodalumab Achieves Clearance as a Rescue Treatment

Despite the many successes of biologics in plaque psoriasis, treatment failure remains a significant problem for many patients and practitioners. Brodalumab has also been evaluated as a rescue therapy in patients who have lost response or developed intolerance to other biologic agents. The data for brodalumab as rescue therapy for ustekinumab and IL-17A inhibitor treatment failures are discussed next.

Ustekinumab is an IL-12/23 inhibitor approved for moderate-to-severe plaque psoriasis.[17] Few studies have shown the utility of brodalumab in patients who experienced inadequate response or intolerance. Langley et al assessed brodalumab rescue in 124 patients who had inadequate responses to ustekinumab vs 149 patients who continued ustekinumab despite no response at week 16.[27] PASI75, PASI90, and PASI100 response rates for the brodalumab rescue group were 72.6%, 58.1%, and 36.3%, respectively, whereas those in the ustekinumab continuation group were 61.7%, 25.5%, and 5.4%, respectively. Furthermore, exposure-adjusted rates of adverse events were similar between the two groups.

Brodalumab rescue therapy was also assessed in patients who were refractory to anti-IL-17A inhibitors. A retrospective study by Gasslitter et al assessed patients with moderate-to-severe psoriasis who did not respond satisfactorily to an IL-17A inhibitor and switched to another biologic in the same class.[28] There were 7 cases of secukinumab switches to brodalumab, of which 4 cases (57%) achieved PASI75, 1 case (14%) achieved PASI50, and 2 cases (28%) did not achieve success by week 12. Ixekizumab was switched to brodalumab in 3 cases of which 2 (66%) achieved PASI75. Kimmel et al also assessed the efficacy of brodalumab in patients who failed anti-IL-17A therapies in moderate-to-severe psoriasis.[29] Failure to an IL-17A agent (ie, secukinumab, ixekizumab) was defined as either lack of PASI75 response or a 50% loss of original improvement by week 12. Thirty-nine patients were enrolled with 34 patients receiving brodalumab and completing all visits through week 16. As-observed results showed 71% of patients achieved sPGA score of 0 (clear) or 1 (almost clear) and 76%, 50%, and 32% achieved PASI75, PASI90, and PASI100, respectively, indicating that the majority of patients who failed IL-17A inhibitors experienced significant improvement in their psoriasis with brodalumab.

Similar findings were noted by Kromer et al who found that ~48% of anti-IL-17A nonresponders achieved PASI75 after switching to brodalumab at week 12.[30] Yeung et al also performed a multicenter retrospective study in Canada of 47 patients who failed to achieve PASI75 with either secukinumab or ixekizumab and switched to brodalumab.[31] At week 16, 61.7%, 46.8%, and 42.5% of patients achieved PASI75, PASI90, and PASI100, respectively. Interestingly, they observed that a significant proportion of patients who previously failed 3 biologics achieved PASI90 with brodalumab.

Brodalumab in the Treatment of Nail, Scalp, and Palmoplantar Psoriasis

Psoriasis involvement of the nail, scalp, and palms/soles further contributes to poor quality of life. With respect to nail psoriasis, a post hoc analysis of phase 3 clinical trials assessing patients with moderate-to-severe nail psoriasis treated with either brodalumab or ustekinumab for 52 weeks found brodalumab to exhibit significantly greater rates of NAPSI 0 (complete clearance of nail psoriasis) at week 12 (7.9%) and week 52 (63.8%) compared to ustekinumab (2.2% and 39.1%, respectively).[4] An open-label, single-center unblinded study also assessed response of severe nail psoriasis of the fingers and toes separately.[32] Brodalumab treatment resulted in statistically significant reductions in NAPSI for bother fingers and toes compared to baseline at weeks 12 and 24. In addition, a real-world case series of 4 patients with psoriatic nail involvement achieved significant or complete clearance after 12 to 20 weeks of treatment.[33]

Regarding scalp involvement, brodalumab exhibited significant improvement rates from baseline in mean Psoriasis Scalp Severity Index (PSSI) scores at week

12 compared to placebo (92.8% vs 14.4%, respectively) in a post hoc analysis of the phase 3 trial.[4] An effect was noted as early as 2 weeks (67.6% vs 6.7%). Similar efficacy was noted at week 12 in a subanalysis of a phase 2 Japanese placebo-controlled trial with mean PSSI improvement being 94.5% vs 12.6% for brodalumab vs placebo, respectively.[34]

Data on efficacy of brodalumab on palmoplantar psoriasis is scarce and exploratory. Nonetheless, a case series by Politou et al assessed brodalumab in 16 patients who failed prior secukinumab treatment and found that 4 out of 4 (100%) patients with palmoplantar pustulosis achieved complete skin clearance at week 16.[35]

Brodalumab Safety and Pharmacovigilance

Despite the safety profile of brodalumab being well elucidated in multiple phase 2/3 studies and US pharmacovigilance reports, there remains a boxed warning regarding suicidal ideation and behavior that is included in the US package insert.[36] Unlike other biologic programs, inclusion of subjects in the brodalumab clinical trials was not based on screening for history of drug abuse, depression, or suicidal behavior.[37]

At the time of this writing, the most recent pharmacovigilance report published in April 2023 summarized 4 years of the most common adverse events from the package insert and those of special interest in the United States from 2017 to 2021.[38] Data were collected from 4019 patients with an estimated exposure of 4563 patient years (PYs).There was a single case of suicide attempt but no causal relationship with brodalumab was established. Since approval, there have been zero completed suicides in the United States. Furthermore, only 4 of 52 cases of depression were determined to be related to brodalumab.

With regard to the most common adverse events (with an incidence of ≥ 1%) listed on the package insert, arthralgia was the most frequently reported (115 events). This is followed by serious infections where 3 of 102 reported cases were deemed to be related to brodalumab. Twenty-six COVID-19 cases were also reported. There were no serious fungal infections. In addition, 37 malignancies were reported in 32 cases, but none were determined to be related to brodalumab.

Cost-Effectiveness

It is important to consider the economic burden of the available treatments in conjunction with that of the disease itself. With the high costs of research and development of biologics, it is not surprising that biologics initially may be expensive and may increase the economic burden on patients and healthcare systems.[39] However, the long-term benefits of effective psoriasis treatment, including improved quality of life and reduced comorbidities, can ultimately lead to cost savings. As such, cost-effectiveness studies of drugs are often considered by payers when making decisions on coverage, formulary position, and budgets.[39] While initial decisions are based on the drug's pre-launch estimated cost, post-launch studies significantly aid in reevaluating a drug's cost-effectiveness and the placement of the drug in formularies.

According to the analysis by the Institute for Clinical and Economic Review (ICER) on the cost-effectiveness of targeted immunomodulatory drugs for the treatment of moderate-to-severe plaque psoriasis, brodalumab was estimated to be the second most cost-effective IL-17 drug (behind secukinumab) and the fourth most

cost-effective therapeutic based on at-approval cost estimates as the study was conducted at the end of 2016 and brodalumab was approved in February 2017. However, an update of the ICER calculations by Hendrix et al in May 2017 based on the updated wholesale acquisition costs estimated brodalumab to be the most cost-effective therapeutic.[5,40]

Feldman et al created an economic model in 2018 to assess the impact of brodalumab on pharmacy budget of US commercial healthcare plans.[41] Prior to brodalumab approval, the total annual pharmacy budget for biologics was estimated at $414,362,647. With the introduction of brodalumab where usage comprised 3% to 30% of moderate-to-severe psoriasis patients, they estimated a reduction of the total annual pharmacy cost to be between $3,698,129 and $36,981,290.

CONCLUSION

Brodalumab, the first-in-class IL-17 receptor inhibitor, is a safe and effective therapeutic for moderate-to-severe plaque psoriasis. Despite no head-to-head comparisons, brodalumab appears to exhibit faster efficacy compared to IL-17A inhibitors. Brodalumab also has demonstrated efficacy in circumstances where patients have failed IL-17A inhibitors and were switched to brodalumab. In addition, brodalumab has been successful for difficult-to-treat areas such as the nails, scalp, palms, and soles. The latest 4-year pharmacovigilance analytics also reveal no new suicide behavior signals attesting to very low risk of use in a population whose quality of life is so significantly affected by widespread psoriasis. Furthermore, economic analysis of brodalumab usage suggests its utility in lowering healthcare costs in the US given its cost-effectiveness. Thus, brodalumab is an excellent addition to the psoriasis toolkit.

DISCLOSURES

Leon Kircik MD has served as either a speaker, consultant, advisor or an investigator for Abbott Laboratories, Abbvie, Allergan, Inc., Almirall, Amgen, Inc., Arcutis, Biogen-Idec, BMS, Boehringer-Ingleheim, Breckinridge Pharma, Celgene, Centocor, Inc., Cellceutix, Cipher, Combinatrix, Connetics Corporation, Coria, Dermavant, Dermira, Dow Pharmaceutical Sciences, Inc., Dr. Reddy's Lab, Eli Lilly, Galderma, Genentech, Inc., GlaxoSmithKline PLC, Idera, Johnson & Johnson, Leo, Maruho, Medicis Pharmaceutical Corp., Merck, Nimbus, Novartis AG, Ortho Dermatologics, PharmaDerm, Pfizer, Promius, Serono (Merck Serono International SA), Stiefel Laboratories, Inc., Sun Pharma, Taro, UCB, Valeant Pharmaceuticals Intl, Ventyx, and XenoPort.

Naiem T. Issa MD PhD has served as a speaker for Ortho Dermatologics.

REFERENCES

1. Vanderpuye-Orgle J, Zhao Y, Lu J, et al. Evaluating the economic burden of psoriasis in the United States. J Am Acad Dermatol. Jun 2015;72(6):961-7.e5. doi:10.1016/j.jaad.2015.02.1099
2. Ghoreschi K, Balato A, Enerbäck C, et al. 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
3. Papp KA, Leonardi C, Menter A, et al. Brodalumab, an anti-interleukin-17-receptor antibody for psoriasis. N Engl J Med. 2012;366(13):1181-9. doi:10.1056/NEJMoa1109017
4. Elewski B, Rich P, Lain E, et al. Efficacy of brodalumab in the treatment of scalp and nail psoriasis: results from three phase 3 trials. J Dermatolog Treat. 2022;33(1):261-265. doi:10.1080/09546634.2020.1749546
5. Hendrix N, Ollendorf DA, Chapman RH, et al. Cost-effectiveness of targeted pharmacotherapy for moderate to severe plaque psoriasis. J Manag Care Spec Pharm. Dec 2018;24(12):1210-1217. doi:10.18553/jmcp.2018.24.12.1210
6. Krueger JG, Fretzin S, Suárez-Fariñas M, et al. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. J Allergy Clin Immunol. Jul 2012;130(1):145-54.e9. doi:10.1016/j.jaci.2012.04.024

7. Bugaut H, Aractingi S. Major role of the IL17/23 axis in psoriasis supports the development of new targeted therapies. Front Immunol. 2021;12:621956. doi:10.3389/fimmu.2021.621956
8. Bianchi E, Rogge L. The IL-23/IL-17 pathway in human chronic inflammatory diseases - new insight from genetics and targeted therapies. Microbes Infect. 2019;21(5-6):246-253. doi:10.1016/j.micinf.2019.06.009
9. Johansen C, Usher PA, Kjellerup RB, et al. Characterization of the interleukin-17 isoforms and receptors in lesional psoriatic skin. Br J Dermatol. 2009;160(2):319-24. doi:10.1111/j.1365-2133.2008.08902.x
10. Nies JF, Panzer U. IL-17C/IL-17RE: Emergence of a unique axis in T(H)17 biology. Front Immunol. 2020;11:341. doi:10.3389/fimmu.2020.00341
11. Simopoulou T, Tsiogkas SG, Zafiriou E, et al Secukinumab, ixekizumab, bimekizumab and brodalumab for psoriasis and psoriatic arthritis. Drugs Today (Barc). 2023;59(3):135-167. doi:10.1358/dot.2023.59.3.3419557
12. Frieder J, Kivelevitch D, Menter A. Secukinumab: a review of the anti-IL-17A biologic for the treatment of psoriasis. Ther Adv Chronic Dis. 2018;9(1):5-21. doi:10.1177/2040622317738910
13. Shelton SK, Bai SR, Jordan JK, et al. Ixekizumab: a review of its use for the management of moderate to severe plaque psoriasis. Ann Pharmacother. Mar 2019;53(3):276-284. doi:10.1177/1060028018799982
14. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175(2):273-86. doi:10.1111/bjd.14493
15. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis–results of two phase 3 trials. N Engl J Med. 014;371(4):326-38. doi:10.1056/NEJMoa1314258
16. Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. N Engl J Med. Jul 28 2016;375(4):345-56. doi:10.1056/NEJMoa1512711
17. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. N Engl J Med. 2015;373(14):1318-28. doi:10.1056/NEJMoa1503824
18. Blauvelt A, Reich K, Tsai TF, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study. J Am Acad Dermatol. 2017;76(1):60-69.e9. doi:10.1016/j.jaad.2016.08.008
19. Bissonnette R, Luger T, Thaçi D, et al. Secukinumab demonstrates high sustained efficacy and a favourable safety profile in patients with moderate-to-severe psoriasis through 5 years of treatment (SCULPTURE Extension Study). J Eur Acad Dermatol Venereol. 2018;32(9):1507-1514. doi:10.1111/jdv.14878
20. Leonardi C, Reich K, Foley P, et al. Efficacy and safety of ixekizumab through 5 years in moderate-to-severe psoriasis: long-term results from the UNCOVER-1 and UNCOVER-2 Phase-3 randomized controlled trials. Dermatol Ther (Heidelb). Jun 2020;10(3):431-447. doi:10.1007/s13555-020-00367-x
21. Lebwohl MG, Blauvelt A, Menter A, et al. Efficacy, safety, and patient-reported outcomes in patients with moderate-to-severe plaque psoriasis treated with brodalumab for 5 years in a long-term, open-label, phase II study. Am J Clin Dermatol. Dec 2019;20(6):863-871. doi:10.1007/s40257-019-00466-2
22. Fried R, Lebwohl M, Bettencourt M, et al. Onset of plaque psoriasis treatment responses with anti-IL-17/IL-23 biologic therapies. J Drugs Dermatol. Aug 1 2022;21(8):854-860. doi:10.36849/jdd.66791
23. Bewley A, Burrage DM, Ersser SJ, et al. 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):763-70. doi:10.1111/jdv.12174
24. Lebwohl M, Cather J, Armstrong A, et al. Recapture rate of brodalumab in patients with a lapse in treatment. J Drugs Dermatol. 2020;19(4):384-387. doi:10.36849/jdd.2020.5026
25. Blauvelt A, Reich K, Warren RB, et al. Secukinumab re-initiation achieves regain of high response levels in patients who interrupt treatment for moderate to severe plaque psoriasis. Br J Dermatol. 2017;177(3):879-881. doi:10.1111/bjd.15656
26. Blauvelt A, Papp KA, Sofen H, et al. Continuous dosing versus interrupted therapy with ixekizumab: an integrated analysis of two phase 3 trials in psoriasis. J Eur Acad Dermatol Venereol. 2017;31(6):1004-1013. doi:10.1111/jdv.14163
27. Langley RG, Armstrong AW, Lebwohl MG, et al. Efficacy and safety of brodalumab in patients with psoriasis who had inadequate responses to ustekinumab: subgroup analysis of two randomized phase III trials. Br J Dermatol. Feb 2019;180(2):306-314. doi:10.1111/bjd.17318

28. Gasslitter I, Kirsten N, Augustin M, et al. Successful intra-class switching among IL-17 antagonists: a multicentre, multinational, retrospective study. Arch Dermatol Res. Jul 2019;311(5):421-424. doi:10.1007/s00403-019-01907-y

29. Kimmel G, Chima M, Kim HJ, et al. Brodalumab in the treatment of moderate to severe psoriasis in patients when previous anti-interleukin 17A therapies have failed. J Am Acad Dermatol. 2019;81(3):857-859. doi:10.1016/j.jaad.2019.05.007

30. Kromer C, Wilsmann-Theis D, Gerdes S, et al. Changing within the same class: efficacy of brodalumab in plaque psoriasis after treatment with an IL-17A blocker - a retrospective multicenter study. J Dermatolog Treat. 2021;32(8):878-882. doi:10.1080/09546634.2020.1716932

31. Yeung J, Vender R, Turchin I, et al. Brodalumab success in patients with moderate-to-severe psoriasis who failed previous interleukin-17A inhibitors. J Am Acad Dermatol. 2021;84(4):1169-1171. doi:10.1016/j.jaad.2020.11.013

32. Gregoriou S, Tsiogka A, Tsimpidakis A, et al. Treatment of nail psoriasis with brodalumab: an open-label unblinded study. J Eur Acad Dermatol Venereol. 2021;35(4):e299-e301. doi:10.1111/jdv.17055

33. Pinter A, Bonnekoh B, Hadshiew IM, et al. Brodalumab for the treatment of moderate-to-severe psoriasis: case series and literature review. Clin Cosmet Investig Dermatol. 2019;12:509-517. doi:10.2147/ccid.S211938

34. Nakagawa H, Niiro H, Ootaki K. Brodalumab, a human anti-interleukin-17-receptor antibody in the treatment of Japanese patients with moderate-to-severe plaque psoriasis: Efficacy and safety results from a phase II randomized controlled study. J Dermatol Sci. 2016;81(1):44-52. doi:10.1016/j.jdermsci.2015.10.009

35. Politou M, Pompou M, Afroditi KI, et al. 18501 Twenty patients with moderate to severe psoriasis successfully treated with brodalumab after a failed treatment with secukinumab. Journal of the American Academy of Dermatology. 2020;83(6):AB214. doi:10.1016/j.jaad.2020.06.946

36. Siliq [package insert]. Bridgewater, NJ: Bausch Health US, LLC; 2020.

37. 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. doi:10.1111/bjd.19132

38. Lebwohl M, Koo J, Leonardi C, et al. Brodalumab: 4-Year US pharmacovigilance report. J Drugs Dermatol. 2023;22(4):419-422. doi:10.36849/jdd.7344

39. Brixner D, Oderda G, Biskupiak J, et al. The challenge of variable costs in decisions based on cost-effectiveness evidence: a case study for brodalumab. Am Health Drug Benefits. 2019;12(1):22-26.

40. Wu JJ, Feldman SR, Rastogi S, et al Comparison of the cost-effectiveness of biologic drugs used for moderate-to-severe psoriasis treatment in the United States. J Dermatolog Treat. 2018;29(8):769-774. doi:10.1080/09546634.2018.1466022

41. Feldman SR, Wu JJ, Rastogi S, et al The budget impact of brodalumab for the treatment of moderate-to-severe plaque psoriasis on US commercial health plans. J Med Econ. 2018;21(5):537-541. doi:10.1080/13696998.2018.1431920

AUTHOR CORRESPONDENCE

Leon Kircik MD

E-mail:..... wedoderm@yahoo.com

JOURNAL OF DRUGS IN DERMATOLOGY
JDD
DRUGS • DEVICES • METHODS