Safety and efficacy of brodalumab for psoriasis after 120 weeks of treatment

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Background: Brodalumab (anti—interleukin-17-receptor antibody) was effective in treating moderate to severe psoriasis in a 12-week, dose-ranging, placebo-controlled trial.

Objective: We sought to evaluate efficacy and safety of long-term brodalumab treatment.

Methods: In this interim analysis at week 120 of an open-label extension study, patients received brodalumab 210 mg every 2 weeks. Protocol amendments reduced the dose (140 mg) in patients weighing 100 kg or less and subsequently increased the dose (210 mg) in patients with inadequate responses. Efficacy was measured by static physician global assessment and 75% or greater, 90% or greater, or 100% improvement in Psoriasis Area and Severity Index score (PASI-75, PASI-90, and PASI-100, respectively).

Results: Of 181 patients, 144 completed week 120. Static physician global assessment scores of clear/almost clear and clear were achieved by 90% and 63% of patients, respectively, at week 12 and by 72% and 51% at week 120. The PASI-75, PASI-90, and PASI-100 response rates at week 12 (95%/85%/63%) were sustained through week 120 (86%/70%/51%). Most commonly reported adverse events were nasopharyngitis (26.5%), upper respiratory tract infection (19.9%), arthralgia (16.0%), and back pain (11.0%). Four patients had grade-2 absolute neutrophil count.

Limitations: There was no control group in this open-label extension.

Conclusion: Brodalumab demonstrated sustained clinical response and an acceptable safety profile through 120 weeks in patients with moderate to severe psoriasis. (J Am Acad Dermatol 2014;71:1183-90.)

Key words: anti—interleukin-17 therapy; brodalumab; clinical trial; efficacy; long-term treatment; open-label extension; psoriasis; safety.

Psoriasis, a chronic T-cell—mediated autoimmune disease that affects up to 3% of the population in the United States,[1,2] has a significant effect on patient well-being in terms of psychiatric, cardiovascular, autoimmune, and other comorbidities.[3-7] Although systemic treatments are

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Supported by Amgen Inc. Brodalumab is being co-developed by Amgen Inc and AstraZeneca/MedImmune.

Disclosure: Dr Papp is a consultant, an investigator, and on the speakers bureau for AbbVie, Amgen, Astellas, Bayer, Boehringer Ingelheim, Celgene, Eli Lilly, Forward, Galderma, Janssen, LEO, Merck, Novartis, Pfizer, Roche, and UCB. Dr Leonardi has served as a consultant, an investigator, and/or speaker for Abbott, Amgen, Celgene, Centocor, Eli Lilly, Galderma, Genentech, Genzyme, GlaxoSmithKline, Incyte, Janssen Biotech, Maruho, Novartis, Novo Nordisk, Pfizer, Schering-Plough, Sirtris, Stiefel, Vascular Biogenics, and/or Wyeth. Dr Menter is on an advisory board for AbbVie, Allergan, Amgen, Boehringer Ingelheim, Genentech, Janssen Biotech, LEO, and Pfizer; is a consultant for AbbVie, Allergan, Amgen, Convoy Therapeutics, Eli Lilly, Janssen Biotech, LEO, Novartis, Pfizer, Syntrix Biosystems, Wyeth, and XenoPort; is an investigator for AbbVie, Allergan, Amgen, ApoPharma, Boehringer Ingelheim, Celgene, Convoy Therapeutics, Eli Lilly, Genentech, Janssen Biotech, LEO, Merck, Novartis, Pfizer, Symbio/Maruho, Syntrix Biosystems, and Wyeth; and is on the speakers bureau for AbbVie, Amgen, Janssen Biotech, LEO, and Wyeth. Drs Milmont, Kricorian, Nirula, and Klekotka are employees and shareholders of Amgen. Dr Thompson is a former employee of Amgen and is a shareholder of Amgen.

Supplemental tables are available at http://www.jaad.org.

Accepted for publication August 21, 2014.

Reprints not available from the authors.

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Published online October 10, 2014.

0190-9622/$36.00

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http://dx.doi.org/10.1016/j.jaad.2014.08.039

available, unmet medical needs remain for long-term psoriasis treatments with favorable safety and efficacy profiles.[8]

T helper 17 cells and their signature cytokine interleukin (IL)−17 are implicated in psoriasis.[9-11] Brodalumab, a human anti−IL-17-receptor A monoclonal antibody that antagonizes IL-17A, IL-17F, IL-17A/F, and IL-17E (IL-25) activity,[12,13] was efficacious in a phase-II study of patients with moderate to severe plaque psoriasis, demonstrating early onset of action with statistically significant improvements as early as week 2.[14] At week 12, 82% of the patients in the brodalumab 210-mg group achieved 75% or greater improvement in Psoriasis Area and Severity Index (PASI) score (PASI-75) and 62% of patients achieved complete skin clearance (100% improvement in PASI score [PASI-100]).[14] None of the patients in the placebo group achieved a PASI-75 or -100 response.[14] The current study (ClinicalTrials.gov identifier NCT01101100) is an interim analysis at treatment week 120 of a 264-week open-label extension (OLE) of the previously reported brodalumab study (NCT00975637).[14]

CAPSULE SUMMARY

- Brodalumab was effective in patients with moderate to severe psoriasis in a 12-week, dose-ranging, placebo-controlled study.
- Continuous maintenance therapy through 120 weeks of treatment with brodalumab produced robust and durable clinical response rates.
- Adverse events reported through week 120 were similar to those reported during the double-blind dose-ranging study.

METHODS

Study design and treatment

This phase-II OLE study was designed to evaluate the long-term efficacy and safety of brodalumab in patients with moderate to severe plaque psoriasis (Fig 1).[14] All patients who enrolled in the OLE received brodalumab subcutaneously at OLE baseline, at OLE weeks 1 and 2, and then every 2 weeks (Q2W) for up to 264 weeks. At OLE baseline, patients who had previously received brodalumab restarted brodalumab after a hiatus of 6 weeks or longer based on timing of the last dose (week 8 [280 mg every 4 weeks] or week 10 [70, 140, and 210 mg Q2W]) and the 4-week follow-up period in the phase-II study. Patients who had previously received placebo initiated brodalumab for the first time.

All patients initially received brodalumab 210 mg; after a protocol amendment, the dose was reduced to 140 mg in patients weighing 100 kg or less to align with a potential phase-III dosing regimen. For patients with an inadequate response to brodalumab 140 mg, a subsequent amendment allowed the dose to be increased back to 210 mg. We report data herein for a planned interim analysis after all continuing patients reached week 120. All data through either week 144 or the data cutoff (March 26, 2013), whichever occurred first, were included in the analyses (first-patient enrollment date: December 9, 2009).

Patients

Patients had completed the previously reported double-blind placebo-controlled study before entering this extension study.[14] Patients were enrolled at 23 international sites, and the study protocol was approved by the institutional review board or ethics committee at each participating site.[14] Eligibility criteria have previously been described.[14] Patients eligible for the OLE had completed the week-16 visit of the parent study and had no serious adverse events (AEs) considered related to investigational product.

Efficacy and safety evaluations

Efficacy evaluations included the percentage of patients with a static physician global assessment (sPGA) score of 0 and sPGA score of 0 or 1; the percentage of patients achieving PASI-75, 90% or greater improvement in PASI score (PASI-90), and PASI-100; percentage improvement in PASI score; and the percentage of body surface area affected by psoriasis (body surface area involvement). The sPGA is a 6-point scale with scores ranging from 0 for clear or no apparent disease to 5 for severe disease. Patient-reported outcomes included the Dermatology Life Quality Index (DLQI) and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36v2) mental and physical component scores.

Safety end points included treatment-emergent AEs and serious AEs, graded according to the National Cancer Institute Common Terminology Criteria for AEs version 4.03,[15] and changes in laboratory parameters (hematology, chemistry, and urinalysis). AEs of interest, including neutropenia, infections, injection-site reactions, and hypersensitivity, were also summarized. Blood was collected at baseline, at weeks 4 and 12, every 12 weeks to week 48, and every 24 weeks thereafter for anti-brodalumab antibody analysis using 2 validated

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