Long-term Efficacy, Safety, and Patient-Reported Outcomes in a Phase 2 Study of Brodalumab

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INTRODUCTION

- Brodalumab is a fully human anti–interleukin-17 receptor A monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis
- Brodalumab demonstrated rapid and robust levels of skin clearance in a 12-week, double-blind, phase 2 study in patients with psoriasis[1,2]

OBJECTIVE

- To evaluate the long-term efficacy and safety of brodalumab in an open-label extension (OLE) of the phase 2 study

METHODS

- In the parent study, patients were randomized to brodalumab (70, 140, 210, or 280 mg) or placebo for 12 weeks[1]
- All patients in the OLE initially received brodalumab 210 mg every 2 weeks (Q2W)
  - Dose reduction to brodalumab 140 mg Q2W was later allowed in patients weighing ≤100 kg, along with a subsequent dose increase to brodalumab 210 mg Q2W in patients with an inadequate response to brodalumab 140 mg Q2W
- Efficacy was assessed by psoriasis area and severity index 75% improvement response (PASI 75) and PASI 100 (observed data analysis)
  - Efficacy data were analyzed at weeks 12, 48, 96, 168, 216, and 264
- Other assessments included the percentage of patients with a dermatology life quality index (DLQI) score of 0 or 1 ("DLQI responder")
- Safety was reviewed in all patients who received ≥1 dose of brodalumab using the incidence of treatment-emergent adverse events (TEAEs) and the exposure-adjusted incidence of TEAEs

RESULTS

Patient population

- A total of 181 patients (117 men and 64 women; mean [standard deviation] age, 42.7 [12.2] years; 90% white) entered the OLE; 107 patients had an efficacy evaluation at week 264
- Median duration of brodalumab exposure was 264 (interquartile range, 200-274) weeks

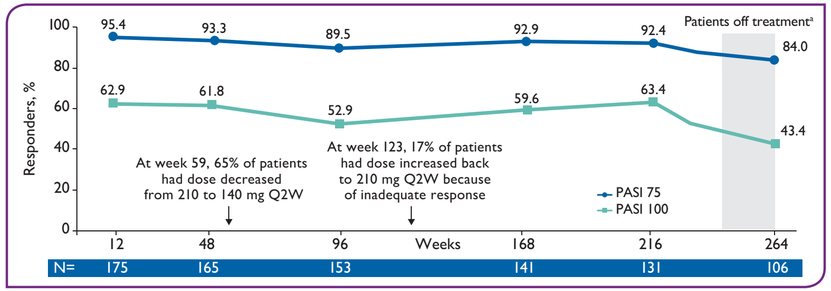
Efficacy

- Efficacy with brodalumab was maintained from week 12 up to week 264, with PASI 75 responses consistently ≥80% and PASI 100 responses consistently ≥40% (Figure 1)
  - There was a decrease in response at week 264 (final study visit), when patients had been off treatment for ≥6 weeks

Patient-reported outcomes

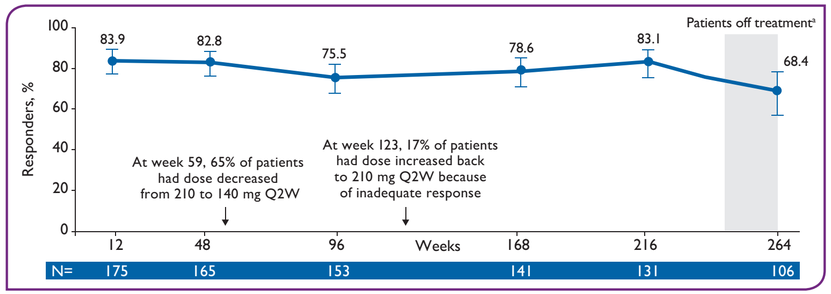
- The percentage of patients receiving brodalumab who had a DLQI score of 0 or 1 was 83.9% at week 12 and 68.4% at week 264 (Figure 2)
- A greater percentage of patients with PASI 100 responses had a DLQI score of 0 or 1 at week 264 (96.4% [27 of 28 patients]) than those with PASI 90 to <100 responses (85.7% [6 of 7 patients]) or PASI 75 to <90 responses (40.0% [2 of 5 patients]; Figure 3)

Figure 1. Rate of skin clearance response by PASI 75 and PASI 100 in patients who received any dose of brodalumab through week 264.



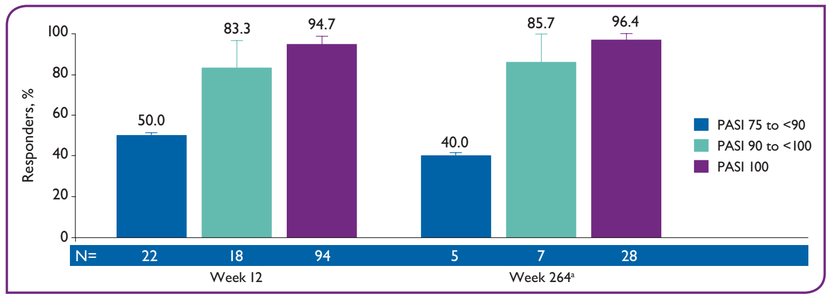
N, number of patients who had a valid measurement value at the specified week; PASI 75 and 100, psoriasis area and severity index 75% and 100% improvement response. Observed data analysis. [a]At week 264, patients had been off treatment for ≥6 weeks.

Figure 2. Percentage of DLQI responders (defined as patients with DLQI score of 0 or 1).



DLQI, dermatology life quality index; N, number of patients who had a valid measurement value at the specified week. Error bars are the 95% confidence interval. [a]At week 264, patients had been off treatment for ≥6 weeks.

Figure 3. DLQI responders (defined as patients with DLQI score of 0 or 1) stratified by skin clearance response.



DLQI, dermatology life quality index; N, number of patients who had a valid measurement value at the specified week. Error bars are the 95% confidence interval. [a]At week 264, patients had been off treatment for ≥6 weeks.

Safety

- No new safety signals emerged in the OLE period
- Over all study years, TEAEs occurred in 177 patients; grade ≥3 TEAEs occurred in 41 patients (23%), and 29 patients (16%) had ≥1 serious TEAE
  - The most common TEAEs included nasopharyngitis, upper respiratory tract infection, and arthralgia (29%, 24%, and 20% of patients, respectively)
- The exposure-adjusted event rate per 100 patient-years (number of events/total patient-years of exposure through end of study × 100) of TEAEs generally decreased over time (Table 1)
  - The most frequent adverse events of interest included nervous system disorder, injection site reaction, psychiatric disorder (depression, suicidal ideation), and oropharyngeal candidiasis

Table 1. Exposure-Adjusted Event Rates of TEAEs Among All Patients Who Received Any Dose of Brodalumab

	Year 1 (N=181)	Year 2 (N=181)	Year 3 (N=181)	Year 4 (N=181)	Year 5 (N=181)	Year 6 (N=181)
Total PY of exposure	172.9	330.1	475.2	611.0	725.7	731.7
Number of TEAEs (exposure-adjusted event rate per 100 PY)[a]						
All TEAEs	748 (432.6)	1154 (349.6)	1373 (288.9)	1565 (256.1)	1750 (241.1)	1770 (241.9)
Grade ≥2	380 (219.8)	593 (179.6)	733 (154.3)	863 (141.2)	997 (137.4)	1014 (138.6)
Grade ≥3	18 (10.4)	29 (8.8)	37 (7.8)	49 (8.0)	59 (8.1)	62 (8.5)
Serious TEAEs	13 (7.5)	18 (5.5)	22 (4.6)	31 (5.1)	40 (5.5)	41 (5.6)
TEAEs of interest						
Nervous system disorder	29 (16.8)	51 (15.4)	62 (13.0)	78 (12.8)	90 (12.4)	91 (12.4)
Injection site reaction	28 (16.2)	38 (11.5)	40 (8.4)	40 (6.5)	41 (5.6)	41 (5.6)
Psychiatric disorder	19 (11.0)	27 (8.2)	32 (6.7)	44 (7.2)	49 (6.8)	49 (6.7)
Oropharyngeal candidiasis	17 (9.8)	23 (7.0)	28 (5.9)	34 (5.6)	41 (5.6)	41 (5.6)
Hypersensitivity event	8 (4.6)	12 (3.6)	12 (2.5)	12 (2.0)	12 (1.7)	12 (1.6)
Depression	4 (2.3)	4 (1.2)	6 (1.3)	7 (1.1)	9 (1.2)	9 (1.2)
Serious infectious episode	4 (2.3)	6 (1.8)	6 (1.3)	7 (1.1)	8 (1.1)	8 (1.1)
Ischemic heart disease	0 (0.0)	0 (0.0)	1 (0.2)	4 (0.7)	7 (1.0)	7 (1.0)
Neutropenia	1 (0.6)	1 (0.3)	1 (0.2)	1 (0.2)	1 (0.1)	1 (0.1)
Suicide self-injury	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
Ischemic cerebrovascular event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Crohn's disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

PY, patient-years; TEAE, treatment-emergent adverse event. Multiple occurrences of the same event for a patient are counted as multiple events. [a]Exposure-adjusted event rate per 100 PY calculated as number of events/total PY of exposure through end of study × 100.

CONCLUSIONS

- **Brodalumab demonstrated high levels of skin clearance efficacy, improved dermatology quality of life scores, and was well tolerated through ~5 years of long-term treatment**
- **Complete skin clearance (PASI 100) with brodalumab was associated with improved quality of life relative to high levels of efficacy without complete skin clearance (PASI 75 to <100)**

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References: 1. Papp et al. *N Engl J Med.* 2012;366:1181-1189. **2.** Papp et al. *J Am Acad Dermatol.* 2014;71:1183-1190.