Long-term Efficacy of Brodalumab for the Treatment of Moderate-to-Severe Psoriasis: Data From a Pivotal Phase 3 Clinical Trial

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INTRODUCTION

- Brodalumab is a fully human anti–interleukin-17 receptor A monoclonal antibody that antagonizes the action of specific inflammatory cytokines involved in psoriasis[1]
- Three pivotal phase 3 clinical trials demonstrated the efficacy and safety of brodalumab through 52 weeks in patients with moderate-to-severe psoriasis (AMAGINE-1/-2/-3)[1,2]
  - Brodalumab exhibited superior efficacy vs ustekinumab, with a faster onset of response and a similar safety profile
  - Data in this poster are from AMAGINE-2

OBJECTIVE

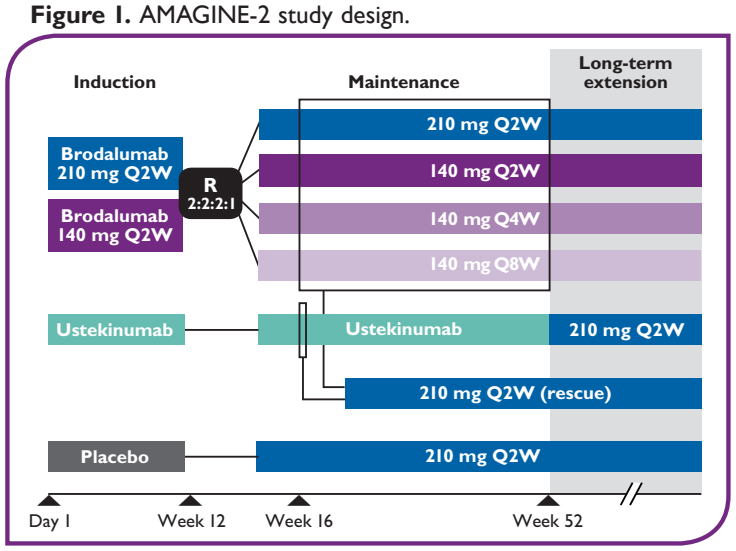
- To evaluate the long-term efficacy and safety of brodalumab in patients with moderate-to-severe plaque psoriasis through 120 weeks

METHODS

Study design

- AMAGINE-2 was a 52-week, randomized, double-blind, placebo- and active comparator–controlled clinical trial
  - Data from this analysis were derived from a long-term open-label extension study through 120 weeks
- Patients received brodalumab 210 or 140 mg every 2 weeks (Q2W), ustekinumab, or placebo during a 12-week induction phase, which was followed by a maintenance phase through week 52 (Figure 1)

Figure 1. AMAGINE-2 study design.



Q2W, every 2 weeks (with an additional loading dose 1 week after initiation of brodalumab); Q4W, every 4 weeks; Q8W, every 8 weeks; R, randomized.

- During the maintenance phase, patients receiving brodalumab were re-randomized to receive a different dose and interval of brodalumab (140 or 210 mg Q2W, Q4W, or Q8W), patients receiving ustekinumab continued on ustekinumab, and patients receiving placebo were switched to brodalumab 210 mg Q2W
  - At week 16, patients from all brodalumab and ustekinumab groups without adequate response (single static physician's global assessment [sPGA] score ≥3 or persistent sPGA score of 2 over ≥4 weeks) were eligible for rescue with brodalumab 210 mg Q2W
- At week 52, patients who received brodalumab during the maintenance phase continued to receive their maintenance dose of brodalumab, and patients who received ustekinumab switched to brodalumab 210 mg Q2W
- Efficacy data are for patients who received brodalumab 210 mg Q2W (the US Food and Drug Administration–approved dose) at any point through week 120 of the long-term extension phase, including patients who received
  - Placebo during the induction phase
  - Ustekinumab during the maintenance phase
  - Brodalumab 140 or 210 mg Q2W during the maintenance phase
  - Rescue treatment during the maintenance phase
- A further subanalysis of efficacy data from patients who received any dose of brodalumab in the induction phase and brodalumab 210 mg Q2W during the maintenance and long-term extension phases is presented
- Safety data are for all patients who received ≥1 dose of brodalumab at any point in the study

Endpoints/Assessments

- Skin clearance was monitored by the sPGA and the psoriasis area and severity index (PASI)
- Safety was assessed by monitoring exposure-adjusted treatment-emergent adverse event rate per 100 patient-years

RESULTS

Patient demographics and baseline disease characteristics

- Most patients were male, with a mean (standard deviation) age of 44.6 (12.8) years (Table 1)

Table 1. Baseline Characteristics

	Full analysis set (N=1831)
Age, mean (SD), y	44.6 (12.8)
Sex, n (%)	
Male	1258 (68.7)
Female	573 (31.3)
Disease duration of psoriasis, mean (SD), y	18.6 (12.2)
sPGA score, n (%)	
3	994 (54.3)
4	723 (39.5)
5 (very severe)	114 (6.2)

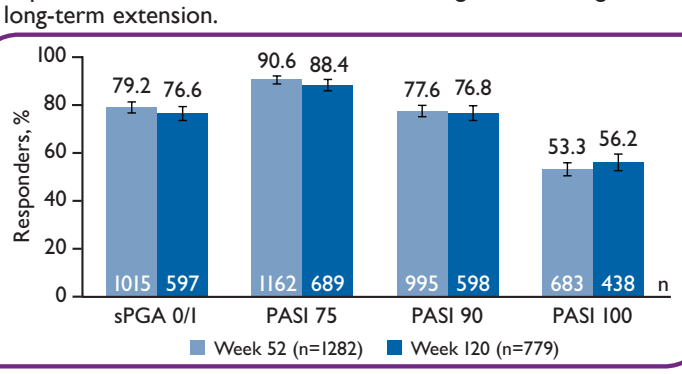
SD, standard deviation; sPGA, static physician's global assessment.

- A total of 1392 patients entered the long-term extension phase on brodalumab 210 mg Q2W, and 1282 patients had a valid measurement at week 52

Efficacy

- Skin clearance response rates at weeks 52 and 120 were similar in patients who received brodalumab 210 mg Q2W during the long-term extension (Figure 2)

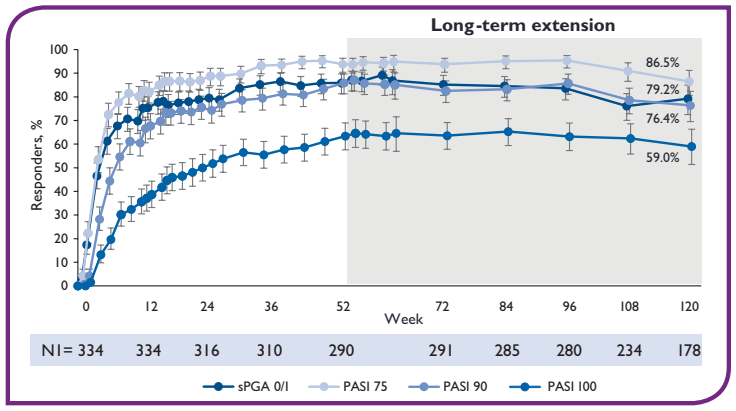
Figure 2. Skin clearance response rates at weeks 52 and 120 in patients who received brodalumab 210 mg Q2W during the long-term extension.



Error bars show the 95% confidence interval. n, number of patients who were responders; PASI 75, 90, and 100, psoriasis area and severity index 75%, 90%, and 100% improvement; sPGA 0/1, static physician's global assessment score of 0 or 1.

- In patients who received any dose of brodalumab in the induction phase and brodalumab 210 mg Q2W during the maintenance and long-term extension phases, rates of achieving sPGA 0/1, PASI 75% improvement (PASI 75), PASI 90, and PASI 100 were maintained from weeks 54 to 120 (Figure 3)
- Patients who received continuous brodalumab throughout the entire study had a higher rate of achieving PASI 100 compared with patients who received placebo or ustekinumab during the induction phase

Figure 3. Patients who received continuous brodalumab and achieved sPGA 0/1, PASI 75, PASI 90, and PASI 100 response through week 120.



Error bars show the 95% confidence interval. N1, number of patients who had a valid measurement value at the specified week; PASI 75, 90, and 100, psoriasis area and severity index 75%, 90%, and 100% improvement; sPGA 0/1, static physician's global assessment score of 0 or 1.

Safety

- A total of 1790 patients received ≥1 dose of brodalumab, with a total time of exposure of 3228.5 years (Table 2)

Table 2. Exposure-Adjusted Event Rates of Patients Who Received ≥1 Dose of Brodalumab Through the End of the Study

n (r)	Brodalumab (all patients) (patient-years = 3228.5) (N=1790)
All TEAEs	9909 (306.9)
Serious AEs	247 (7.7)
AEs leading to drug discontinuation	103 (3.2)
Deaths	1 (0.1)
Most common AEs (>250 events overall)	
Nasopharyngitis	620 (19.2)
Upper respiratory tract infection	499 (15.5)
Arthralgia	295 (9.1)
Headache	288 (8.9)

AE, adverse event; n, number of AEs; r, exposure-adjusted event rate per 100 patient-years (n/patient-year*100); TEAE, treatment-emergent AE.

- The safety profile of brodalumab was consistent with that observed in shorter-term studies, and no new safety signals were identified

CONCLUSIONS

- **Treatment with brodalumab resulted in substantial psoriatic lesion clearing for >2 years in most patients with moderate-to-severe psoriasis**
- **Skin clearance response rates, as determined by sPGA 0/1, PASI 75, PASI 90, and PASI 100, were maintained from weeks 52 to 120 in patients who received brodalumab 210 mg Q2W**
- **Patients receiving continuous treatment with brodalumab had higher rates of PASI 100 compared with patients who received placebo or ustekinumab during the induction phase**

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References: 1. Lebwohl et al. *N Engl J Med.* 2015;373:1318-1328. **2.** Papp et al. *Br J Dermatol.* 2016;175:273-286.