Long-term Efficacy and Safety of Brodalumab in Patients With Psoriasis Whose Disease Did Not Respond to Prior Biologics

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INTRODUCTION

- Patients with psoriasis who experience treatment failure to, or whose disease does not respond to, biologic therapies over time may encounter medical or economic consequences, including higher mean total healthcare-related costs and increased use of other medications[1]
- Brodalumab is a fully human anti–interleukin-17 receptor A monoclonal antibody that is efficacious in treating moderate-to-severe psoriasis[2]
- It is crucial to understand the efficacy of subsequent biologic treatment in individuals whose disease did not respond to initial biologic treatment

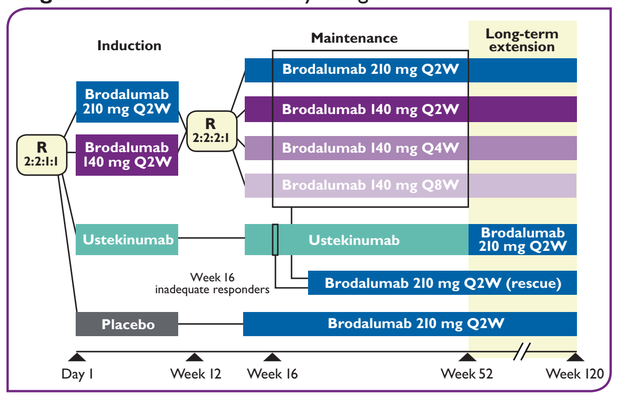
OBJECTIVES

- To assess long-term efficacy and safety of brodalumab in 2 multicenter randomized clinical trials (AMAGINE-2/-3; ClinicalTrials.gov identifiers: NCT01708603, NCT01708629) in patients with moderate-to-severe plaque psoriasis whose disease did not respond to 1, 2, or ≥3 prior biologics[3]

METHODS

- In AMAGINE-2/-3, patients were initially randomized to brodalumab 140 or 210 mg every 2 weeks, ustekinumab, or placebo during a 12-week induction phase (Figure 1)
  - At week 12, patients who received brodalumab were re-randomized to either the same or a different brodalumab regimen, patients receiving ustekinumab continued on ustekinumab, and patients receiving placebo were switched to brodalumab 210 mg every 2 weeks
- At week 52, all patients entered the long-term extension phase and received brodalumab
- 408 patients from AMAGINE-2/-3 who received any dose of brodalumab through week 120 were included in this post-hoc analysis, which comprised
  - 160 patients with a lack of response to 1 biologic
  - 112 patients with a lack of response to 2 biologics
  - 136 patients with a lack of response to ≥3 biologics
- Skin clearance was monitored by psoriasis area and severity index 75% improvement (PASI 75), PASI 90, and PASI 100 responses
- Safety was summarized by exposure-adjusted treatment-emergent adverse event (TEAE) rates

Figure 1. AMAGINE-2/-3 study design.



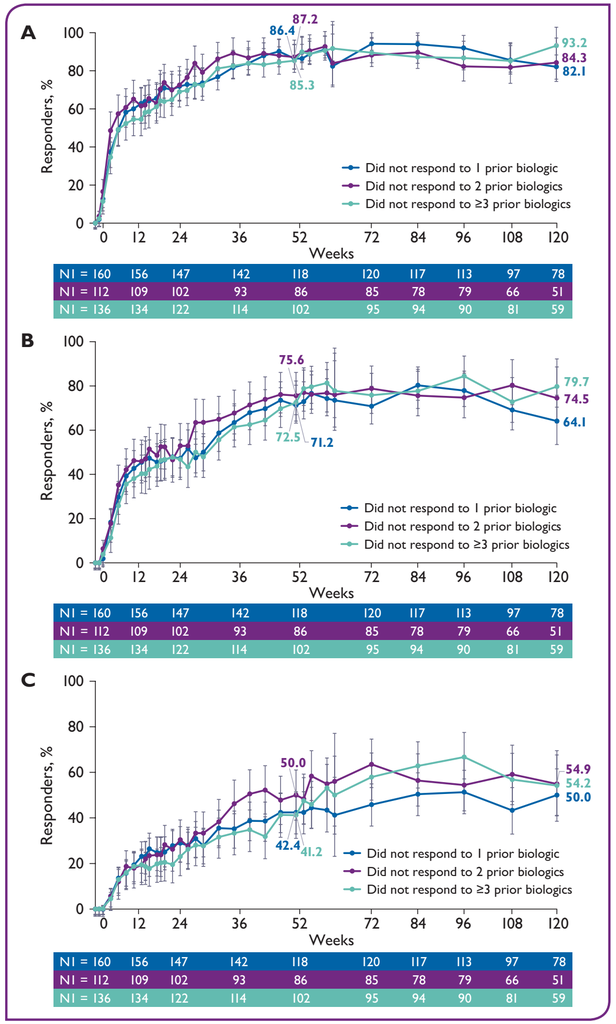
R, randomization; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks.

RESULTS

Efficacy

- Among patients whose disease did not respond to 1, 2, or ≥3 prior biologics, skin clearance rates were comparable from weeks 52 to 120 in those achieving PASI 75 (Figure 2A), PASI 90 (Figure 2B), and PASI 100 (Figure 2C)
- In an observed analysis at week 52, PASI 75 response rates in patients whose disease did not respond to 1, 2, or ≥3 prior biologics were 86.4%, 87.2%, and 85.3%, respectively
  - PASI 90 response rates were 71.2%, 75.6%, and 72.5%, respectively
  - PASI 100 response rates were 42.4%, 50.0%, and 41.2%, respectively
- At week 120, observed PASI 75 response rates were 82.1%, 84.3%, and 93.2% in patients whose disease did not respond to 1, 2, or ≥3 prior biologics, respectively
  - PASI 90 response rates were 64.1%, 74.5%, and 79.7%, respectively
  - PASI 100 response rates were 50.0%, 54.9%, and 54.2%, respectively

Figure 2. PASI 75 **(A)**, PASI 90 **(B)**, and PASI 100 **(C)** responses in patients whose disease did not respond to 1, 2, or ≥3 prior biologics.



Error bars indicate 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.

Safety

- Across all years, exposure-adjusted TEAE rates per 100 patient-years in patients receiving brodalumab whose disease did not respond to 1, 2, or ≥3 prior biologics were 359.0, 297.6, and 383.2, respectively (Table 1)

Table 1. Exposure-Adjusted Rates of TEAEs in Patients Who Received Any Dose of Brodalumab

	Did not respond to 1 prior biologic N=160; 269.4 PY	Did not respond to 2 prior biologics N=112; 189.2 PY	Did not respond to ≥3 prior biologics N=136; 215.0 PY
Grade ≥2	535 (198.6)	317 (167.6)	430 (200.0)
Grade ≥3	37 (13.7)	24 (12.7)	32 (14.9)
Serious AEs	23 (8.5)	11 (5.8)	10 (4.7)
Fatal AEs	1 (0.4)	0	0

AE, adverse event; n, number of adverse events; N, number of patients; PY, total patient-years of exposure; TEAE, treatment-emergent adverse event. Values are the number of AEs (exposure-adjusted event rate per 100 patient-years).

CONCLUSIONS

- **Skin clearance rates were comparable in patients whose disease did not respond to 1, 2, or ≥3 prior biologics through week 120**
- **These data demonstrate that brodalumab is efficacious and well tolerated for long-term treatment of moderate-to-severe psoriasis in patients with lack of response to prior biologic therapies, including those with lack of response to ≥3 prior biologics**

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References:

1. Foster et al. *J Manag Care Spec Pharm*. 2016;22:396-405.
2. Siliq [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America, LLC; 2017.
3. Lebwohl et al. *N Engl J Med*. 2015;373:1318-1328.