Brodalumab Versus Ustekinumab in Obese Participants With Moderate-to-Severe Plaque Psoriasis

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OBJECTIVE

- To evaluate clinical outcomes of brodalumab treatment in obese versus nonobese participants with moderate-to-severe plaque psoriasis using data from phase 3 randomized controlled studies (AMAGINE-1/-2/-3)

CONCLUSION

- Regardless of body mass index (BMI), brodalumab demonstrated sustained efficacy in participants with moderate-to-severe plaque psoriasis, with no new safety signals

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References: 1. Bremmer et al. *J Am Acad Dermatol.* 2010;63:1058-1069. **2.** Siliq [package insert]. Bausch Health US, LLC; 2020. **3.** van Voorhees et al. Poster presented at: Fall Clinical Dermatology Conference; October 12-15, 2017; Las Vegas, NV. **4.** Hsu et al. *Br J Dermatol.* 2020;182:880-888.

SYNOPSIS

- Obesity is associated with psoriasis severity and decreased efficacy of psoriasis therapy[1]
- Brodalumab is a human interleukin-17 receptor A antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adult participants who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies[2]
- Psoriasis treatment in patients with obesity presents unique challenges because these individuals may show reduced response to therapies or be more prone to certain adverse effects[1]

METHODS

- Efficacy and safety of brodalumab were investigated in three phase 3, multicenter, randomized trials of participants with moderate-to-severe plaque psoriasis (AMAGINE-1, AMAGINE-2, and AMAGINE-3)
- In AMAGINE-1, participants were randomized to receive brodalumab 210 mg or placebo every 2 weeks (Q2W) for 12 weeks and then were rerandomized to receive brodalumab 210 mg Q2W or placebo for up to 52 weeks
- In AMAGINE-2/-3, participants were randomized to receive brodalumab 210 mg Q2W or ustekinumab (45 mg in participants weighing ≤100 kg and 90 mg in participants weighing >100 kg) for 12 weeks; at week 12, participants receiving brodalumab were rerandomized, and participants receiving ustekinumab continued ustekinumab
- Subgroups included in this post hoc analysis comprised obese (BMI ≥30 kg/m^2) and nonobese participants (BMI <30 kg/m^2) who received brodalumab 210 mg Q2W (AMAGINE-1/-2/-3) or ustekinumab (AMAGINE-2/-3) continuously through 52 weeks
- Outcomes included psoriasis area and severity index 90% and 100% improvement (PASI 90 and 100) and treatment-emergent adverse events (TEAEs)

RESULTS

AMAGINE-1

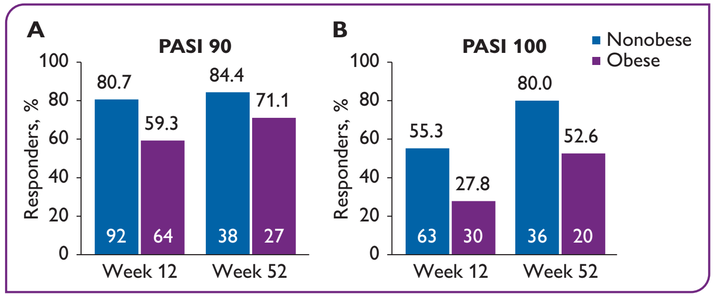
Participant Characteristics

- AMAGINE-1 included 108 obese and 114 nonobese participants receiving brodalumab[3]
  - Most participants were male, with a mean age of 48.0 years for obese participants and 44.7 years for nonobese participants
  - Average BMI was 36.7 kg/m^2 for obese participants and 25.7 kg/m^2 for nonobese participants

Skin Clearance

- At week 12, 59.3% and 27.8% of obese participants receiving brodalumab achieved PASI 90 and 100, respectively (Figure 1)
  - Rates further improved by week 52 (PASI 90: 71.1%; PASI 100: 52.6%)
  - At both time points, nonobese participants achieved higher rates of PASI 90 and 100 compared with obese participants

Figure 1. Nonobese and obese participants who achieved (A) PASI 90 and (B) PASI 100 at weeks 12 and 52 in AMAGINE-1.[3]



PASI 90 and 100, psoriasis area and severity index 90% and 100% improvement. Values shown within bars represent the number of responders.

Safety

- Through 52 weeks, 388.7 TEAEs per 100 patient-years were reported among nonobese participants continuously treated with brodalumab 210 mg Q2W compared with 370.8 TEAEs per 100 patient-years among obese participants (Table)

Table. Exposure-Adjusted Treatment-Emergent Adverse Event Rates by Treatment and Body Weight Category

	AMAGINE-1[3]		AMAGINE-2/-3[4]			
n (r)	Obese brodalumab (n=164)	Nonobese brodalumab (n=181)	Obese brodalumab (n=91)	Nonobese brodalumab (n=157)	Obese ustekinumab (n=131)	Nonobese ustekinumab (n=185)
All TEAEs	558 (388.7)	474 (370.8)	328 (366.3)	607 (404.4)	533 (420.6)	659 (366.5)
SAEs	10 (7.0)	17 (13.3)	9 (10.0)	14 (9.3)	12 (9.5)	9 (5.0)

n, number of TEAEs; Q2W, every 2 weeks; r, exposure-adjusted event rate per 100 patient-years (n/patient-year × 100); SAE, serious adverse event; TEAE, treatment-emergent adverse event. Multiple occurrences of the same event for a patient are counted as multiple events. Data are presented from the first dose of the study through to the end of the study in the safety-evaluable subset of participants. The brodalumab treatment group includes participants who received brodalumab 210 mg Q2W throughout the study. The ustekinumab treatment group includes participants who received ustekinumab throughout the study.

AMAGINE-2/-3

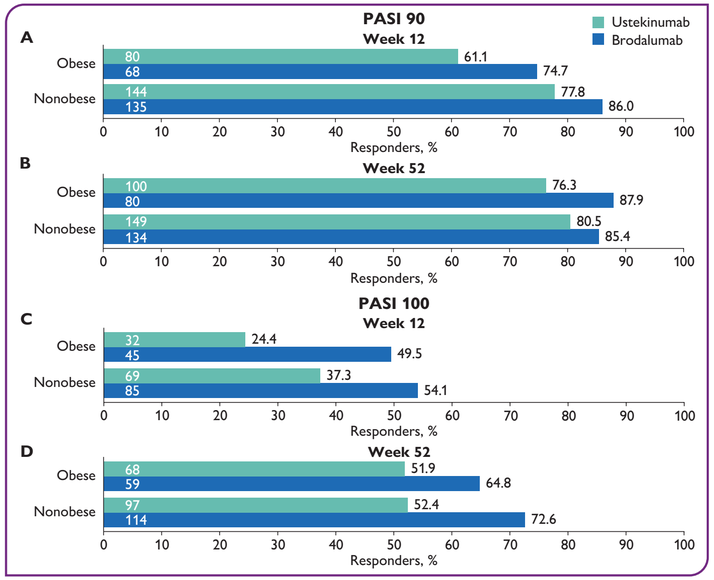
Participant Characteristics

- AMAGINE-2/-3 included 91 obese and 157 nonobese participants receiving brodalumab and 131 obese and 185 nonobese participants receiving ustekinumab[4]
  - Most participants were male, and obese participants were generally older than nonobese participants (approximate average age ~48 years vs ~43 years)
  - Average BMI was approximately 35.6 kg/m^2 for obese participants and 25.1 kg/m^2 for nonobese participants

Skin Clearance

- For obese participants receiving brodalumab, rates of PASI 90 and 100 were 74.7% and 49.5%, respectively, at week 12 (Figure 2)
- These rates further improved by week 52 (PASI 90: 87.9%; PASI 100: 64.8%) and were higher compared with those of obese participants receiving ustekinumab (PASI 90: 76.3%; PASI 100: 51.9%)

Figure 2. Achievement of skin clearance at (A, C) week 12 and (B, D) week 52 by treatment subgroup and BMI category in AMAGINE-2/-3.[4]



The brodalumab treatment group includes participants who received brodalumab 210 mg Q2W throughout the study. The ustekinumab treatment group includes participants who received ustekinumab throughout the study. Nonresponder imputation was used to impute missing data. Values shown within bars represent the number of responders. BMI, body mass index; PASI 90 and 100, psoriasis area and severity index 90% and 100% improvement; Q2W, every 2 weeks.

- Regardless of BMI category, the percentages of PASI 90 and 100 responders were greater with brodalumab compared with ustekinumab
- By week 52, PASI responses were similar among nonobese and obese participants within each respective treatment group

Safety

- Through 52 weeks, TEAEs per 100 patient-years were reported in participants receiving brodalumab (AMAGINE-2/-3, obese: 366.3, nonobese: 404.4) and ustekinumab (AMAGINE-2/-3, obese: 420.6, nonobese: 366.5; Table)