Efficacy and Safety of Brodalumab in Obese Patients With Moderate-to-Severe Plaque Psoriasis

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INTRODUCTION

- Brodalumab is a fully human anti–interleukin-17 receptor A (IL-17RA) monoclonal antibody indicated for the treatment of moderate-to-severe plaque psoriasis[1]
- Efficacy and safety of brodalumab were evaluated in a phase 3, multicenter, randomized, double-blind, placebo-controlled study (AMAGINE-1)[1]
- There is a well-established association between psoriasis and obesity, with the risk of psoriasis directly related to body mass index (BMI)[2,3]
  - Risk estimate (95% CI) for psoriasis in those with BMI ≥30 kg/m^2 was 1.9 (1.2-2.8), as determined from an analysis of an Italian cohort[3]
- Obese patients with psoriasis often experience decreased efficacy and increased susceptibility to certain side effects of therapeutic agents, making effective treatment in this population challenging[2]

OBJECTIVE

- To evaluate the efficacy and safety of brodalumab in nonobese and obese patients with moderate-to-severe plaque psoriasis

METHODS

Study design

- Efficacy and safety of brodalumab were investigated in a phase 3, multicenter, randomized trial of patients with moderate-to-severe plaque psoriasis (AMAGINE-1)
  - Patients were randomized to receive brodalumab 210 mg or placebo every 2 weeks (Q2W) for 12 weeks
  - After 12 weeks, patients were re-randomized to receive brodalumab 210 mg Q2W or placebo for up to 52 weeks
- On the basis of BMI, patients were categorized as nonobese (BMI <30 kg/m^2) or obese (BMI ≥30 kg/m^2)
- Comparisons between nonobese and obese patients were made among patients who received continuous treatment with brodalumab 210 mg Q2W through 52 weeks

Endpoints/Assessments

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

RESULTS

Patient demographics and baseline disease characteristics

- Most patients were male, with an approximate mean (standard deviation) age of 45.8 (13.3) years for nonobese patients and 47.0 (12.4) years for obese patients (Table 1)

Table 1. Baseline Characteristics

	Nonobese		Obese	
	Placebo (n=130)	Brodalumab 210 mg Q2W (n=114)	Placebo (n=89)	Brodalumab 210 mg Q2W (n=108)
Age, mean (SD), y	47.4 (13.7)	44.7 (11.9)	46.1 (12.5)	48.0 (12.3)
Sex, n (%)				
Male	101 (77.7)	79 (69.3)	59 (66.3)	82 (75.9)
Female	29 (22.3)	35 (30.7)	30 (33.7)	26 (24.1)
Weight, mean (SD), kg	78.6 (12.2)	75.7 (12.5)	107.2 (17.0)	108.0 (20.5)
BMI, mean (SD), kg/m^2	26.1 (2.6)	25.7 (2.9)	36.4 (5.8)	36.7 (7.2)

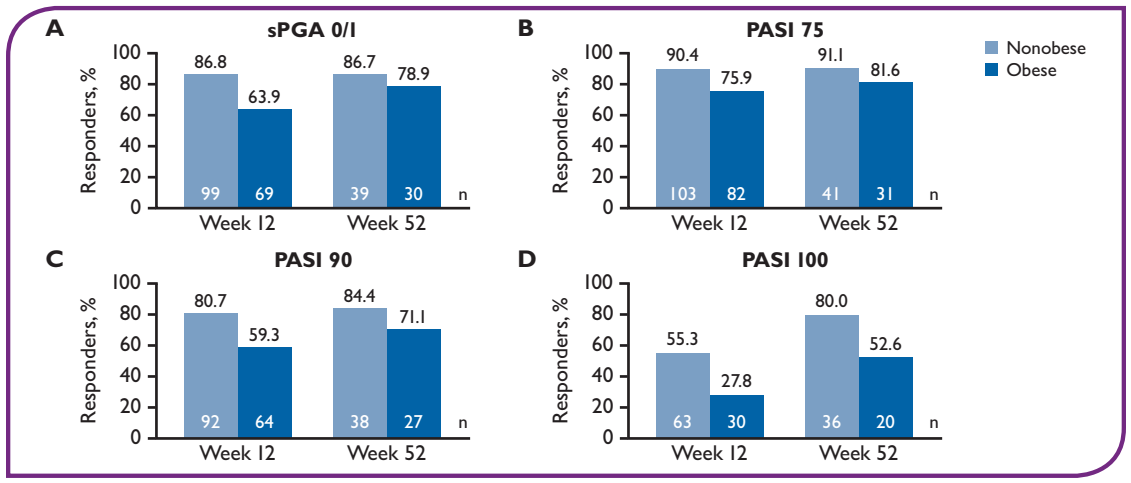
BMI, body mass index; Q2W, every 2 weeks; SD, standard deviation.

- Of 659 total patients at baseline, 54.6% (n=360) were nonobese and 45.4% (n=299) were obese
- Weight and BMI were similar between the placebo and brodalumab groups within the nonobese and obese groups

Efficacy

- In a post hoc comparison of patients receiving continuous brodalumab 210 mg Q2W, rates of achieving sPGA score of 0 or 1 (sPGA 0/1), 75% improvement in PASI (PASI 75), PASI 90, and PASI 100 were higher among nonobese patients than obese patients at weeks 12 and 52 (Figure)
- The percentage of patients achieving PASI 100 increased from week 12 to week 52 in both nonobese and obese patients

Figure. Nonobese and obese patients who achieved **(A)** sPGA 0/1, **(B)** PASI 75, **(C)** PASI 90, and **(D)** PASI 100 at weeks 12 and 52.



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.

- Obese patients had a larger increase in response rates of skin clearance as measured by sPGA 0/1, PASI 75, PASI 90, and PASI 100 from week 12 to week 52 compared with nonobese patients
- At week 12, 2.3% (3/130), 3.1% (4/130), 1.5% (2/130), and 0.8% (1/130) of nonobese patients receiving placebo achieved sPGA 0/1, PASI 75, PASI 90, and PASI 100, respectively, compared with 0% (0/89), 2.2% (2/89), 0% (0/89), and 0% (0/89) of obese patients (data not shown)
  - Among nonobese and obese patients randomized to the placebo group after week 12, none achieved sPGA 0/1, PASI 75, PASI 90, or PASI 100 at week 52 (data not shown)

Safety

- Through 52 weeks, 388.7 TEAEs per 100 patient-years were reported among nonobese patients continuously treated with brodalumab 210 mg Q2W compared with 370.8 TEAEs per 100 patient-years among obese patients (Table 2)

Table 2. Exposure-Adjusted TEAE Rates Through Week 52

n (r)	Nonobese (n=181)	Obese (n=164)
All TEAEs	558 (388.7)	474 (370.8)
All SAEs	10 (7.0)	17 (13.3)
Deaths	2 (1.4)	1 (0.8)
Infections	174 (121.2)	149 (116.6)
Fungal infections	7 (4.9)	11 (8.6)

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

CONCLUSIONS

- **Higher rates of skin clearance as assessed by sPGA and PASI were associated with brodalumab 210 mg Q2W in nonobese vs obese patients**
- **Rates of complete skin clearance (PASI 100) increased in both nonobese and obese patients with longer duration of treatment with brodalumab 210 mg Q2W (through 52 weeks)**
- **The increase in response rate of skin clearance from week 12 to week 52 in obese patients was greater than that in nonobese patients, suggesting that response rate can be improved with longer treatment in obese patients**

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References: 1. Papp et al. *Br J Dermatol.* 2016;175:273-286. **2.** Bremmer et al. *J Am Acad Dermatol.* 2010;63:1058-1069. **3.** Naldi et al. *J Invest Dermatol.* 2005;125:61-67.