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Efficacy of Guselkumab Through 48 Weeks in Chinese Psoriasis Patients With and Without Metabolic Comorbidities: A Post-Hoc Analysis of a Phase 4 RCT

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Key Takeaways

- **Guselkumab demonstrated high levels of treatment response in Chinese patients with moderate-to-severe psoriasis, regardless of the presence of metabolic comorbidities**
- **These results may help inform treatment decisions for psoriasis in Chinese patients with comorbidities commonly observed in this patient population**

Background

Patients with psoriasis, a chronic immune-mediated inflammatory skin disease, have an increased risk of having metabolic comorbidities compared with the general population.[1,2] Moreover, metabolic comorbidities in patients with psoriasis are associated with a reduced likelihood of achieving optimal Psoriasis Area and Severity Index (PASI) responses[3]

Guselkumab is a fully human monoclonal antibody that targets the p19 subunit of interleukin-23 and is approved for the treatment of moderate-to-severe psoriasis[4]

A recent Chinese post-approval commitment (PAC) phase 4 study showed efficacy and a well tolerated safety profile of guselkumab in Chinese patients with moderate-to-severe psoriasis.[5] However, treatment response to guselkumab in Chinese patients with various metabolic comorbidities has not been evaluated

Objectives

Here we report the results from a post-hoc analysis for guselkumab efficacy through 48 weeks in Chinese patients with moderate-to-severe psoriasis based on patients' metabolic comorbidities at baseline

Methods

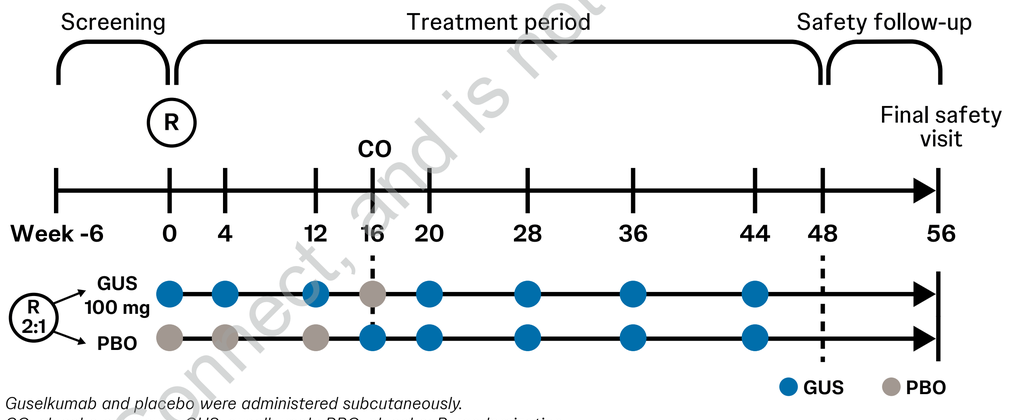
Study Design

- This PAC study (NCT04914429) enrolled patients from 26 sites in China
- Eligible patients were required to have a diagnosis of moderate-to-severe plaque psoriasis, defined by an Investigator's Global Assessment (IGA) score ≥3, Psoriasis Area and Severity Index (PASI) ≥12, and involved body surface area ≥10%, and to be eligible for either systemic therapy or phototherapy
- At baseline, 327 patients were randomized at a 2:1 ratio to receive guselkumab 100 mg (n=217) or placebo (n=110) by subcutaneous injection at Weeks 0, 4, and 12. At Week 16, patients in the placebo group crossed over to receive guselkumab. From Weeks 20 to 44, all patients received guselkumab treatment every 8 weeks (Figure 1)

Statistical Analysis

- All randomized patients were included in this post-hoc analysis
- Subgroup analyses were conducted based on the presence of metabolic comorbidities (i.e., obesity, hyperlipidemia, hypertension, hyperuricemia, and diabetes mellitus) at baseline
- Baseline demographics and disease characteristics between patients with versus without metabolic comorbidities were summarized descriptively
- Averaged responder rates for IGA 0/1 or PASI 90 at Weeks 16 and 48 in subgroups with versus without each metabolic comorbidity were calculated based on 200 multiple imputation datasets

Figure 1: Study design



Guselkumab and placebo were administered subcutaneously.
CO, placebo crossover; GUS, guselkumab; PBO, placebo; R, randomization.

Results

Baseline Demographics and Disease Characteristics of Patients With Versus Without Metabolic Comorbidities

- Among the 327 randomized patients, the most frequently reported metabolic comorbidities were obesity (body mass index ≥28 kg/m^2, n=80, 24.6%), hyperlipidemia (n=73, 22.3%), hypertension (n=69, 21.1%), hyperuricemia (n=41, 12.5%), and diabetes mellitus (n=18, 5.5%)
- Patients' baseline characteristics based on status of metabolic comorbidities are summarized in Table 1
- Patients with metabolic comorbidities, compared with those without metabolic comorbidities, respectively, were more likely to:
  - be older (<45 years: 57.0% vs 68.5%; 45 to <65 years: 37.0% vs 29.0%; ≥65 years: 6.1% vs 2.5%)
  - be male (81.8% vs 76.5%)
  - be heavier (>90 kg: 24.4% vs 1.2%; mean body mass index 27.1 kg/m^2 vs 21.2 kg/m^2)
  - have more severe disease (PASI ≥20: 58.8% vs 53.7%; IGA score of 4: 26.7% vs 23.5%)
  - be naïve to non-biologic systemic treatment for psoriasis (ever used: 32.1% vs 39.5%)

Table 1: Patient demographics and disease characteristics at baseline

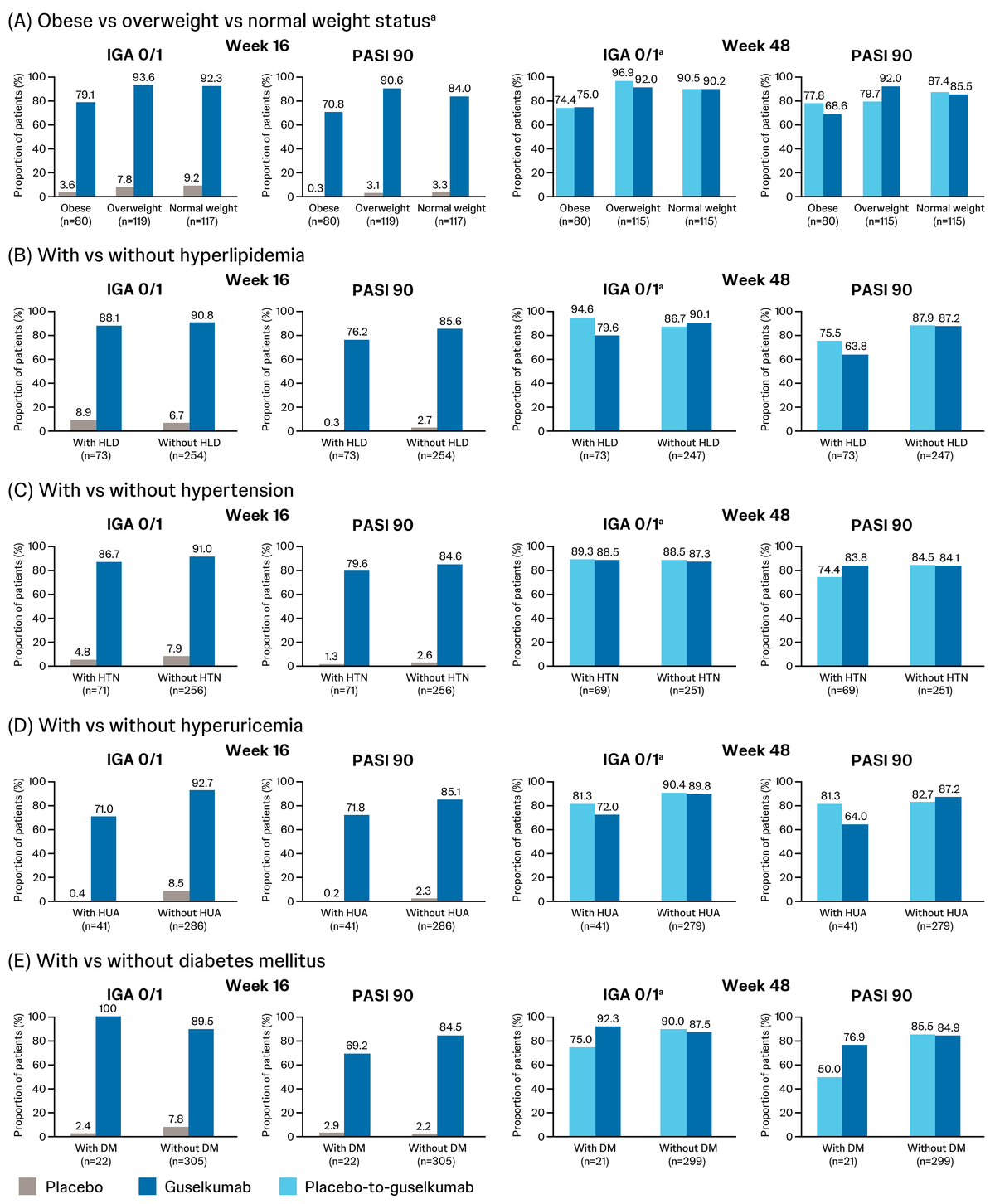
	With Metabolic Comorbidity (N=165)	Without Metabolic Comorbidity (N=162)
Baseline characteristics		
Age, years		
<45	57.0 (94/165)	68.5 (111/162)
45 to <65	37.0 (61/165)	29.0 (47/162)
≥65	6.1 (10/165)	2.5 (4/162)
Gender		
Female	18.2 (30/165)	23.5 (38/162)
Male	81.8 (135/165)	76.5 (124/162)
Body weight, kg		
≤90	75.6 (124/164)	98.8 (159/161)
>90	24.4 (40/164)	1.2 (2/161)
Mean body mass index, kg/m^2 (SD)	27.1 (3.3)[a]	21.2 (2.0)[b]
Mean psoriasis disease duration, years (SD)	11.8 (9.8)	11.8 (9.1)[b]
Mean PASI score (SD)	24.7 (10.5)	23.0 (9.8)
<20	41.2 (68/165)	46.3 (75/162)
≥20	58.8 (97/165)	53.7 (87/162)
Mean body surface area, % (SD)	37.0 (20.9)	33.7 (18.2)
<20	25.5 (42/165)	24.1 (39/162)
≥20	74.6 (123/165)	75.9 (123/162)
IGA score		
Moderate (3)	72.7 (120/165)	76.5 (124/162)
Severe (4)	26.7 (44/165)	23.5 (38/162)
With psoriatic arthritis	12.7 (21/165)	8.6 (14/162)
Prior use of biologics for treatment of psoriasis	6.7 (11/165)	4.9 (8/162)
Prior non-biologic systemic treatment for psoriasis	32.1 (53/165)	39.5 (64/162)

Data are presented as % (n/N) unless otherwise specified. [a]n=164. [b]n=161. SD, standard deviation.

Efficacy of Guselkumab in Patients With Versus Without Metabolic Comorbidities at Baseline

- Response to guselkumab differed numerically between obese versus overweight and normal weight patients (Figure 2A). In the guselkumab group, obese patients had a lower mean response rate versus overweight and normal weight patients, respectively, while mean response rates were generally comparable between overweight and normal weight patients:
  - IGA 0/1: 79.1% versus 93.6% versus 92.3% at Week 16; 75.0% versus 92.0% versus 90.2% at Week 48
  - PASI 90: 70.8% versus 90.6% versus 84.0% at Week 16; 68.6% versus 92.0% versus 85.5% at Week 48
- In the guselkumab group, patients with hyperlipidemia versus those without hyperlipidemia, respectively, achieved a comparable mean IGA 0/1 response rate at Week 16 but had a numerically lower mean IGA 0/1 response rate at Week 48; mean PASI 90 response rates were numerically lower for patients with hyperlipidemia at both Weeks 16 and 48 (Figure 2B):
  - IGA 0/1: 88.1% versus 90.8% at Week 16; 79.6% versus 90.1% at Week 48
  - PASI 90: 76.2% versus 85.6% at Week 16; 63.8% versus 87.2% at Week 48
- In the guselkumab group, patients with hypertension and those without hypertension, respectively, had generally similar mean IGA 0/1 and PASI 90 response rates at Week 16 (IGA 0/1: 86.7% vs 90.1%; PASI 90: 79.6% vs 84.6%) and Week 48 (IGA 0/1: 88.5% vs 87.3%; PASI 90: 83.8% vs 84.1%) (Figure 2C)
- In the guselkumab group, patients with hyperuricemia versus those without hyperuricemia, respectively, had numerically lower mean IGA 0/1 and PASI 90 response rates at Week 16 (IGA 0/1: 71.0% vs 92.7%; PASI 90: 71.8% vs 85.1%) and Week 48 (IGA 0/1: 72.0% vs 89.8%; PASI 90: 64.0% vs 87.2%) (Figure 2D)
- With a limited number of patients having diabetes mellitus in the guselkumab group, inconsistent trends for mean IGA 0/1 and PASI 90 response rates were observed among patients with versus without diabetes mellitus, respectively, at Week 16 (IGA 0/1: 100.0% vs 89.5%; PASI 90: 69.2% vs 84.5%) and Week 48 (IGA 0/1: 92.3% vs 87.5%; PASI 90: 76.9% vs 84.9%) (Figure 2E)

Figure 2: Response to treatment based on patients' metabolic comorbidities at baseline



[a]BMI categories were underweight (<18.5 kg/m^2), normal weight (18.5 to <24 kg/m^2), overweight (24 to <28 kg/m^2), and obese (≥28 kg/m^2).
BMI, body mass index; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; HUA, hyperuricemia.

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