A randomized, double-blind, multicenter study to compare the efficacy, safety, and immunogenicity of a proposed adalimumab biosimilar (GP2017) with originator adalimumab in patients with moderate-to-severe chronic plaque psoriasis

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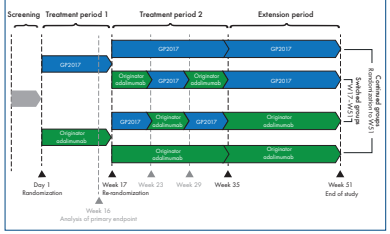
Introduction

- GP2017 is being developed as a proposed biosimilar to originator adalimumab.
  - Extensive state-of-the-art analytical studies have shown that GP2017 and originator adalimumab have identical amino acid sequences, indistinguishable secondary and tertiary structures, the same level of post-translational modifications, and similar *in vitro* functionality.[1]
  - Pharmacokinetic (PK) bioequivalence was demonstrated in phase I PK studies in healthy volunteers, with GP2017 and originator adalimumab having similar clinical safety and immunogenicity profiles.
- The purpose of this phase III confirmatory study (NCT02016105) was to show equivalent efficacy and comparable safety and immunogenicity between GP2017 and originator adalimumab up to 51 weeks in patients with moderate-to-severe chronic plaque psoriasis.
  - Here, data from randomization to Week 17 are presented for patients receiving GP2017 or originator adalimumab.

Study design

- This was a multicenter, randomized, double-blinded, comparator-controlled phase III confirmatory study with four study periods (Figure 1).

Figure 1. Study design



- Adult male and female patients with active, but clinically stable, moderate-to-severe chronic plaque psoriasis were eligible for enrolment if they were ≥18 years of age; had a baseline PASI score of ≥12, an Investigators Global Assessment (IGA) score of ≥3, and a body surface area (BSA) affected by plaque psoriasis of ≥10%; had previously received phototherapy or systemic psoriasis therapy or were candidates for such therapies; had no history of active or latent Hepatitis B and/or C infections or tuberculosis, and had not received prior treatment with adalimumab.
- In treatment period 1, patients were randomized to receive an initial dose of 80 mg subcutaneous GP2017 or originator adalimumab sourced from either the EU or US, followed by 40 mg every other week, starting one week after the initial dose, up to Week 17.

Primary endpoint

- Proportion of patients who achieved a 75% improvement in the psoriasis area and severity index score (PASI 75) at Week 16.
  - Therapeutic equivalence was confirmed if the 95% confidence interval (CI) for the difference in PASI 75 response rates between GP2017 and originator adalimumab for the per-protocol set (PPS) was contained within a margin range of ±18%.

Secondary endpoints

- Percentage change from baseline until Week 16 in the continuous PASI score, with equivalence concluded if the 95% CI was within ±15%
- PASI 50, PASI 90 and PASI 100 response rates over time
- Percentage change from baseline in PASI score at each visit
- IGA response rate: proportion of patients with a score of 0 (clear) or 1 (almost clear) on the IGA scale (0–4) and ≥2 point improvement from baseline
- Health-related quality of life (HRQoL) with regard to relative changes in the dermatology life quality index (DLQI) and EuroQol 5-dimension health (EQ-5D) status questionnaire from baseline to Weeks 11, 16, and 17
- Safety, immunogenicity, tolerability and local tolerance

Results

Patients

- The full analysis set (FAS) comprised 231 patients who received GP2017 and 234 patients who received originator adalimumab.
  - Of these, 197 and 196 patients completed the study up to Week 16 with no major protocol deviations and were included in the PPS.
- Patient demographics and disease characteristics were balanced across both treatment groups (Table 1).

Table 1. Baseline patient and disease characteristics (FAS)

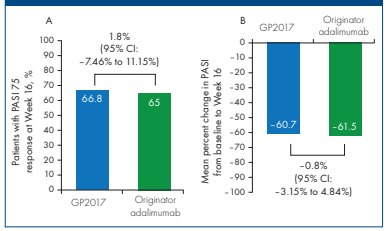
	GP2017 (n=231)	Originator adalimumab (n=234)
Age (years), mean (SD)	45.6 (14.2)	46.9 (14.1)
Male, n (%)	142 (61.5)	142 (60.7)
Race, n (%)		
Caucasian	196 (84.8)	201 (85.9)
Black	14 (6.1)	9 (3.8)
Asian	3 (1.3)	5 (2.1)
Other	18 (7.8)	19 (8.1)
BMI (kg/m²), mean (SD)	31.4 (8.1)	30.7 (7.5)
Duration since diagnosis (years), mean (SD)	15.3 (12.6)	16.9 (14.7)
PASI score, mean (SD)	19.9 (8.6)	20.2 (7.7)
IGA score, n (%)		
3=Moderate	152 (65.8)	154 (65.8)
4=Severe	79 (34.2)	80 (34.2)
% BSA affected, mean (SD)	28.9 (17.1)	29.7 (15.6)
Presence of psoriatic arthritis, n (%)	52 (22.5)	46 (19.7)
Prior systemic psoriasis therapy, n (%)		
Biologic	54 (23.4)	44 (18.8)
Nonbiologic	72 (31.2)	81 (34.6)

BMI, body mass index; BSA, body surface area; IGA, Investigator's Global Assessment; PASI, psoriasis area and severity index; SD, standard deviation

Efficacy

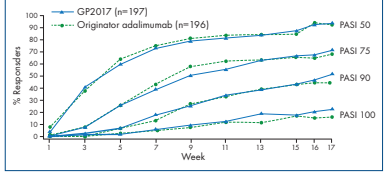
- In the PPS, the PASI 75 response rate difference at Week 16 was 1.8% (66.8% for GP2017 and 65.0% for originator adalimumab).
  - As the 95% CI was contained within the prespecified margin range of ±18%, equivalent efficacy between GP2017 and originator adalimumab was confirmed (Figure 2A).
- Using a mixed model repeated measures method, mean percent change (improvement) from baseline up to Week 16 in PASI score was 60.7% for GP2017 and 61.5% with originator adalimumab in the PPS.
  - The 95% CI for the difference in the percentage change from baseline in PASI up to Week 16 was contained within ±15%; thereby showing therapeutic equivalence (Figure 2B).

Figure 2. Primary and key secondary efficacy analyses (PPS)



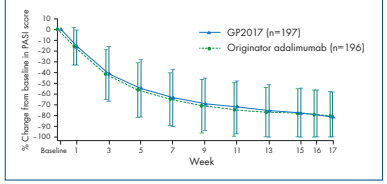
- PASI response rates for GP2017 and originator adalimumab were similar over time (Figure 3).

Figure 3. PASI response rates over time (PPS)



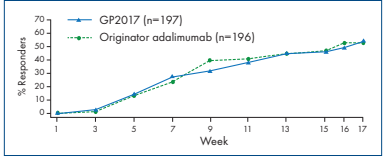
- Mean percent changes in PASI score from baseline were similar (Figure 4)

Figure 4. Mean percent change from baseline in PASI score (PPS)



- IGA response rates increased over time and were similar in both treatment groups (Figure 5).

Figure 5. IGA response rates over time (PPS)



HRQoL

- The proportion of patients in the PPS reporting a DLQI of 0 or 1 (no effect at all on patient's life) was similar between the treatment groups at all time points (Table 2).
- Mean EQ visual analog scale scores, which range from 0 to 100 with lower scores indicating greater impairment in HRQoL, were also similar (Table 2).

Table 2. Improvements in HRQoL (PPS)

	DLQI score of 0 or 1, n/n (%)		EQ visual analog scale score (SD)	
	GP2017	Originator adalimumab	GP2017	Originator adalimumab
Baseline	4/197 (2.0)	8/195 (4.1)	69.9 (22.1)	70.0 (23.2)
Week 11	79/194 (40.7)	79/193 (40.9)	77.5 (18.8)	78.2 (20.1)
Week 16	98/191 (51.3)	88/191 (46.1)	80.6 (17.0)	80.2 (20.0)
Week 17	97/192 (50.5)	93/192 (48.4)	80.5 (17.1)	80.7 (19.7)

Safety

- Among all patients who received ≥1 dose of study drug (safety analysis set; SAF), adverse events (AEs) occurred in 50.2% and 52.6% of patients treated with GP2017 and originator adalimumab, respectively; most of which were mild or moderate in severity (Table 3).
- The proportions of patients with severe AEs, serious AEs (SAEs), treatment-related SAEs, AEs of special interest, AEs requiring study drug interruption, and discontinuations due to AEs were low across both treatment groups.

Table 3. Incidence of AEs from randomization to Week 17 (SAF)

Patients, n (%)	GP2017 (n=231)	Originator adalimumab (n=234)
≥1 AE	116 (50.2)	123 (52.6)
≥1 severe AE	3 (1.3)	10 (4.3)
≥1 SAE	3 (1.3)	10 (4.3)
≥1 treatment-related AE	33 (14.3)	28 (12.0)
≥1 treatment-related SAE	1 (0.4)	3 (1.3)
AE of special interest	13 (5.6)	17 (7.3)
Treatment interruption due to AE	5 (2.2)	4 (1.7)
Discontinuation due to AE	4 (1.7)	7 (3.0)
Died	0 (0.0)	0 (0.0)

- Infections/infestations were most common, with nasopharyngitis most frequently reported (Table 4).

Table 4. AEs by system organ class and preferred term (≥2% in any treatment group) from randomization to Week 17 (SAF)

System organ class Preferred term Patients, n (%)	GP2017 (n=231)	Originator adalimumab (n=234)
Infections and infestations	55 (23.8)	56 (23.9)
Nasopharyngitis	13 (5.6)	15 (6.4)
Upper respiratory tract infection	11 (4.8)	9 (3.8)
Sinusitis	8 (3.5)	7 (3.0)
General disorders and administration site conditions	23 (10.0)	15 (6.4)
Injection site erythema	9 (3.9)	3 (1.3)
Fatigue	5 (2.2)	6 (2.6)
Musculoskeletal and connective tissue disorders	22 (9.5)	15 (6.4)
Back pain	6 (2.6)	3 (1.3)
Arthralgia	6 (2.6)	2 (0.9)
Nervous system disorders	19 (8.2)	14 (6.0)
Headache	11 (4.8)	8 (3.4)
Respiratory, thoracic and mediastinal disorders	15 (6.5)	15 (6.4)
Gastrointestinal disorders	14 (6.1)	27 (11.5)
Diarrhea	2 (0.9)	9 (3.8)
Skin and subcutaneous tissue disorders	12 (5.2)	15 (6.4)
Injury, poisoning and procedural complications	9 (3.9)	8 (3.4)
Investigations	8 (3.5)	9 (3.8)
Psychiatric disorders	6 (2.6)	5 (2.1)
Metabolism and nutrition disorders	5 (2.2)	7 (3.0)
Neoplasms benign, malignant and unspecified	4 (1.7)	5 (2.1)
Blood and lymphatic system disorders	3 (1.3)	5 (2.1)
Vascular disorders	2 (0.9)	7 (3.0)
Reproductive system and breast disorders	2 (0.9)	5 (2.1)

Immunogenicity

- 36.8% patients treated with GP2017 and 34.1% of patients treated with originator adalimumab were anti-drug antibody (ADA)-positive at least once up to Week 17.
- Approximately 80% of ADA were neutralizing.

Conclusions

- Week 17 results of this phase III confirmatory study show equivalent efficacy of GP2017 and originator adalimumab.
- Safety and immunogenicity profiles of GP2017 and originator adalimumab were also similar and consistent with clinical experience with originator adalimumab.

Reference

1. Schiestl M, Roesli C. *Am J Gastroenterol* 2016; 111:S260–S335

Disclosure Statement

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