Sponsor

Sandoz
Sandoz Inc., Hexal AG

Generic Drug Name

Adalimumab

Trial Indication(s)

Plaque-type Psoriasis

Protocol Number

GP17-301 / GPN017A2301

Protocol Title

A Randomized, Double-blind, Multicenter Study to Demonstrate Equivalent Efficacy and to Compare Safety and Immunogenicity of a Biosimilar Adalimumab (GP2017) and Humira in Patients With Moderate to Severe Chronic Plaque-type Psoriasis (ADACCESS)

Clinical Trial Phase

Phase III

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: 18 December 2013

Primary Completion Date: 6 July 2015

Study completion Date: 25 February 2016

Reason for Termination (If applicable)

N/A

Study Design/Methodology

Multicenter, randomized, double-blind, comparator-controlled, confirmatory efficacy and safety (Phase III) study to assess equivalent efficacy, safety, and immunogenicity of the proposed biosimilar GP2017 and Humira up to 51 weeks in patients with moderate to severe chronic plaque-type psoriasis. In addition, the long-term effects including safety and immunogenicity up to Week 51 and the effect of repeated switching between GP2017 and Humira were to be analyzed.

The study consisted of 4 study periods:

1. Screening Period started once the patient had provided their written informed consent to participate in the study. It ended at the time of the randomization visit.

2. Treatment Period 1 (Randomization to Week 17) started at the time of randomization and ended prior to study drug administration at Week 17. Eligible patients were randomized in a 1:1 ratio into either the GP2017 or the Humira treatment groups. Randomization was stratified by body weight ("<90 kg" or "≥90 kg"), prior systemic psoriasis therapy ("no prior systemic therapy" or "any prior systemic therapy"), and region (US or EU). Patients received either GP2017 or Humira s.c. as a loading dose of 80 mg at the randomization visit and subsequently a dose of 40mg every other week starting at Week 1 for another 8 doses in total until Week 15.

3. Treatment Period 2 (Week 17 to Week 35) started at Week 17 and ended at Week 35, prior to the administration of the next dose of study treatment. Only patients who achieved at least a PASI50 response at Week 16, qualified for entry into Treatment Period 2. At Week 17, the qualifying patients from both treatment groups were re-randomized in a 2:1 ratio to either remain on their initial study treatment or to receive GP2017 or Humira during 3 alternating periods of 6 weeks each, up t to Week 35. The re-randomization was stratified by region (US or EU) only.

4. The Extension Period (Week 35 to Week 51) started at the time point of the Week 35 study drug administration and ended at Week 51. During this period, patients received the same study treatment as in Treatment Period 1.

Centers

76 study centers in 4 countries Bulgaria (4), France (2), Slovakia (3), and the US (67) in total screened 661 patients. Thereof 73 sites randomized a total of 465 patients into the study.

Objectives:

Primary objective (Treatment Period 1: Randomization to Week 17)
The primary objective of this study was to demonstrate equivalent efficacy of GP2017 and Humira in patients with moderate to severe chronic plaque-type psoriasis with respect to the psoriasis area severity index (PASI) 75 response rate at Week 16, defined as the proportion of patients achieving a reduction of 75% or more of the PASI score at Week 16 compared to baseline. This primary objective was demonstrated by comparing all Humira treated patients and GP2017 treated patients.

Key Secondary objective (Treatment Period 1: Randomization to Week 17)
The key secondary objective was to compare the relative change from until Week 16 in the continuous PASI score of patients treated with GP2017 or Humira. This key secondary objective was demonstrated by comparing all Humira treated patients and GP2017 treated patients.

Main secondary objectives (for the entire study)
- the comparison of PASI scores; PASI50, PASI75, PASI90 and PASI100 response rates;
- investigator's global assessment (IGA) and health related quality of life (dermatology life quality index [DLQI],

- the comparison of the clinical safety and tolerability of GP2017 and Humira as assessed by adverse event (AE) monitoring
- the comparison of immunogenicity as determined by measuring the rate of anti-drug antibody (ADA) formation against GP2017 and Humira.

Test Product (s), Dose(s), and Mode(s) of Administration

GP2017 was administered as subcutaneous injection at a loading dose of 80 mg on Day 1, and followed by 40 mg every other week (eow) starting one week after the initial dose.

Statistical Methods

For the primary and key secondary objectives to be met, equivalence had to be demonstrated for both treatment comparisons: comparing all Humira treated patients and all GP2017 treated patients (using a 95% Confidence Interval (CI)). Therefore no adjustment for multiplicity was required. The analysis of the primary endpoint PASI75 response rate at Week 16, was based on the per-protocol set (PPS), which consisted of all patients who completed the study until Week 16 without major protocol deviations. PASI75 response rates at Week 16 for the comparison GP2017 versus (vs.) Humira were analyzed by logistic regression including the treatment group ("GP2017" or "Humira"), body weight (<90 or ≥90kg), and prior systemic therapy (no/any) as factors in the model.
The covariate-adjusted difference in proportions and the corresponding 2-sided CI (95% for GP2017 vs. Humira) for the difference were estimated. Therapeutic equivalence in terms of PASI75 response rate was concluded if the CI (95% for GP2017 vs. Humira) for the difference in the PASI75 rates was contained within the interval [-18%; 18%].
The key secondary endpoint, the percentage change from baseline in the PASI score up to Week 16, was analyzed both by applying a mixed model repeated measures (MMRM) model and by examining the mean average treatment effect (ATE) per patient using an analysis of covariance (ANCOVA) model. Both models, for the comparison GP2017 vs. Humira, included the treatment group ("GP2017" or "Humira"), body weight (<90 or ≥90kg), and prior systemic therapy (no/any) as factors and the baseline PASI score as a continuous covariate.
Factors for visit and treatment-by-visit interaction were additionally included in the MMRM model and an unstructured covariance matrix was assumed. Adjusted means for each treatment group, the difference between the adjusted means, and the corresponding 2-sided CI (95% for GP2017 vs. Humira) for the difference were estimated. Therapeutic equivalence in terms of the percentage change from baseline in the PASI score up to Week 16 was concluded if the exact CI (95% for GP2017 vs. Humira) for the difference was contained within the interval [-15%; 15%].

All other secondary efficacy, safety, and immunogenicity parameters were analyzed using frequency tables or descriptive statistics.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Men or women at least 18 years of age at time of screening
- Chronic plaque-type psoriasis diagnosed for at least 6 months before randomization
- Moderate to severe psoriasis as defined at baseline by:
  - PASI score of 12 or greater
  - Investigator´s Global Assessment score of 3 or greater (based on a scale of 0 - 4) and,
  - Body Surface Area affected by plaque-type psoriasis of 10% or greater
- Chronic plaque-type psoriasis patients who have previously received phototherapy or systemic psoriasis therapy at least once or who are candidates for such therapies in the opinion of the investigator.

Exclusion Criteria:

- Forms of psoriasis other than chronic plaque-type
- Drug-induced psoriasis
- Ongoing use of prohibited psoriasis treatments
- Previous exposure to adalimumab
- Active ongoing inflammatory diseases other than psoriasis that might confound the evaluation of the benefit of treatment with adalimumab

Participant Flow Table

Patient disposition by treatment group – Randomization to Week 17 Full Analysis Set (FAS)

	GP2017	Humira
	N=231	N=234

	n (%)	n (%)
Randomized	231 (100.0)	234 (100.0)
Completed Treatment Period 1	201 (87.0)	201 (85.9)
Discontinued during Treatment Period 1	30 (13.0)	33 (14.1)
Reason for discontinuation		
Subject/guardian decision	15 (6.5)	11 (4.7)
Lost to follow-up	6 (2.6)	4 (1.7)
Lack of efficacy	4 (1.7)	2 (0.9)
Adverse event [a]	3 (1.3)	5 (2.1)
Protocol deviation [b]	2 (0.9)	8 (3.4)
Physician decision	0 (0.0)	2 (0.9)
Pregnancy	0 (0.0)	1 (0.4)
Re-randomized to Treatment Period 2	189 (81.8)	190 (81.2)

Sorted by descending frequency in the GP2017 group.

eCRF=electronic case report form; FAS=full analysis set; n=number of patients in treatment group

[a] Recorded as per Treatment period completion eCRF.

[b] Patients did not meet selection criteria

Patient disposition by individual group – Week 17 to Week 35 (Treatment Period 2 (TP2) +Extension Period (EP) FAS)

	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Re-randomized	63 (100.0)	127 (100.0)	63 (100.0)	126 (100.0)
Completed Treatment Period 2	57 (90.5)	116 (91.3)	59 (93.7)	112 (88.9)
Discontinued during Treatment Period 2	6 (9.5)	11 (8.7)	4 (6.3)	14 (11.1)
Reason for discontinuation				

	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Subject/guardian decision	3 (4.8)	1 (0.8)	1 (1.6)	7 (5.6)
Lack of efficacy	2 (3.2)	6 (4.7)	3 (4.8)	2 (1.6)
Lost to follow-up	1 (1.6)	0 (0.0)	0 (0.0)	1 (0.8)
Adverse event [a]	0 (0.0)	4 (3.1)	0 (0.0)	1 (0.8)
Death	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Non-compliance with study treatment	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Continue to Extension Period	52 (82.5)	109 (85.8)	56 (88.9)	106 (84.1)

The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2. Sorted by descending frequency in the Humira to GP2017 group.

eCRF=electronic case report form; n=number of patients in group; TP2+EP FAS=full analysis set Treatment Period 2 and Extension Period

[a] Recorded as per Treatment Period completion eCRF.

Patient disposition by individual group – Week 35 to Week 51 (EP FAS)

	Humira to GP2017 N=52 n (%)	Continued Humira N=109 n (%)	GP2017 to Humira N=56 n (%)	Continued GP2017 N=106 n (%)
Entered Extension Period	52 (100.0)	109 (100.0)	56 (100.0)	106 (100.0)
Completed Extension Period	47 (90.4)	104 (95.4)	50 (89.3)	100 (94.3)
Discontinued during Extension Period	5 (9.6)	5 (4.6)	6 (10.7)	6 (5.7)
Reason for discontinuation				
Subject/guardian decision	2 (3.8)	2 (1.8)	2 (3.6)	2 (1.9)

	Humira to GP2017 N=52 n (%)	Continued Humira N=109 n (%)	GP2017 to Humira N=56 n (%)	Continued GP2017 N=106 n (%)
Adverse event [a]	2 (3.8)	0 (0.0)	1 (1.8)	0 (0.0)
Lack of efficacy	1 (1.9)	3 (2.8)	1 (1.8)	1 (0.9)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.9)
New therapy for study indication	0 (0.0)	0 (0.0)	1 (1.8)	1 (0.9)
Non-compliance with study treatment	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)

The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2. Sorted by descending frequency in the Humira to GP2017 group.

eCRF=electronic case report form; EP FAS=full analysis set during the Extension Period; n=number of patients in treatment group

[a] Recorded as per Treatment Period completion eCRF.

Baseline Characteristics

Demographic summary by treatment group at baseline (FAS)

		GP2017 N=231	Humira N=234
Age[1] (years)	Mean	45.6	46.9
	SD	14.16	14.09
	Median	45.0	47.0
	Min, max	18, 81	18, 84
Sex – n (%)	Male	142 (61.5)	142 (60.7)
	Female	89 (38.5)	92 (39.3)
Race – n (%)	Caucasian	196 (84.8)	201 (85.9)
	Black	14 (6.1)	9 (3.8)
	Asian	3 (1.3)	5 (2.1)
	Native American	4 (1.7)	4 (1.7)

		GP2017 N=231	Humira N=234
	Pacific Islander	0 (0.0)	1 (0.4)
	Unknown	3 (1.3)	0 (0.0)
	Other	11 (4.8)	14 (6.0)
Ethnicity – n (%)	East Asian	1 (0.4)	2 (0.9)
	Hispanic or Latino	50 (21.6)	53 (22.6)
	Mixed ethnicity	20 (8.7)	13 (5.6)
	Russian	3 (1.3)	3 (1.3)
	South Asian	2 (0.9)	0 (0.0)
	Southeast Asian	0 (0.0)	3 (1.3)
	West Asian	0 (0.0)	1 (0.4)
	Other	108 (46.8)	102 (43.6)
	Unknown	18 (7.8)	23 (9.8)
	Not reported	29 (12.6)	34 (14.5)
Weight[1] (kg)	Mean	92.76	90.95
	SD	26.267	24.231
	Median	88.45	86.59
	Min, max	43.8, 174.6	45.0, 180.6
Weight group[2] – n (%)	<90kg	120 (51.9)	127 (54.3)
	≥90kg	111 (48.1)	107 (45.7)
BMI (kg/m^2)	Mean	31.41	30.72
	SD	8.122	7.484
	Median	29.37	29.75
	Min, max	17.6, 61.2	17.2, 55.8

Summary of Efficacy

Primary Outcome Result(s)

Logistic regression analysis on PASI75 response at Week 16 (primary endpoint analysis) - GP2017 vs. Humira (PPS)

	N	n	Adjusted response rate[1] (SE) [%]	Adjusted response rate difference (SE) GP2017 − Humira [%]	95% CI
GP2017	197	132	66.8 (3.33)	1.8 (4.75)	[-7.46, 11.15]
Humira	196	127	65.0 (3.38)		

To conclude equivalent efficacy, the 95% CI had to be entirely within the interval [-18%, 18%].

CI=confidence interval; N=number of patients per treatment group; n=number of patients per treatment group achieving PASI75 response; PASI=psoriasis area and severity index; PPS=per-protocol set; SE=standard error

[1] Adjusted response rates were estimated using a logistic regression model including treatment, body weight strata, region and prior systemic therapy. The 95% CI for the rate difference was derived based on the normal approximation and standard error computed using the delta method.

Secondary Outcome Result(s)

Statistical analyses of percentage change from baseline in PASI score up to Week 16 - GP2017 vs. Humira (PPS)

	N	n	LS means (SE) [%]	LS means difference (SE) GP2017 − Humira [%]	95% CI for LS means difference [%]
Mean percent change from baseline in PASI score (MMRM)[1]					
GP2017	197	191	-60.7 (1.54)	0.8 (2.03)	[-3.15, 4.84]
Humira	196	192	-61.5 (1.55)		
Mean ATE of percent change from baseline in PASI score (ANCOVA)[2]					
GP2017	197	197	-59.7 (1.59)	1.2 (2.00)	[-2.78, 5.08]
Humira	196	196	-60.8 (1.61)		

ANCOVA=analysis of covariance; ATE=averaged treatment effect; CI=confidence interval; LS=least squares; MMRM=mixed-model repeated measures; N=number of patients per treatment group; n=number of patients with evaluable data per treatment group; PASI=psoriasis area and severity index; PPS=per-protocol set; SE=standard error

[1] LS means, SE and 95% CI were estimated by a Mixed-Effects Repeated Measures (MMRM) model with treatment, visit, treatment-by-visit interaction, body weight strata, region and prior systemic therapy, as fixed factors and baseline PASI score as covariate. An unstructured covariance matrix was used to model the within-patient variance-covariance matrix. No imputation of missing values was performed.

[2] ATE is the weighted average of % change from baseline in PASI scores between Week 1 and Week 16 (weights based on the time interval between two consecutive visits). LS means, SE and 95% CI were estimated using an ANCOVA model with treatment, body weight strata, region and prior systemic therapy as fixed effects and baseline PASI score as covariate. No imputation of missing values was performed.

Proportion of patients with PASI 50, PASI 75, PASI 90, and PASI 100 Response Rates at Week 17 (PPS)

		GP2017 N=197	Humira N=196
% of patients achieving PASI 50	Week 17	93.2	92.8
% of patients achieving PASI 75	Week 17	71.4	68.6
% of patients achieving PASI 90	Week 17	51.6	44.8
% of patients achieving PASI 100	Week 17	21.9	16.5

	GP2017 N=197	Humira N=196
Percentages are calculated based on N', PASI=Psoriasis Area and Severity Index		

Proportion of patients with PASI 50, PASI 75, PASI 90, and PASI 100 Response Rates at Week 35 and Week 51 (PPS)

		Humira to GP2017 N=51	Continued Humira N=115	GP2017 to Humira N=55	Continued GP2017 N=105
% of patients achieving PASI 50	Week 35	95.9	96.4	94.1	96.1
% of patients achieving PASI 50	Week 51	95.3	93.9	95.9	93.7
% of patients achieving PASI 75	Week 35	73.5	73.6	70.6	74.5
% of patients achieving PASI 75	Week 51	76.7	79.6	75.0	84.5
% of patients achieving PASI 90	Week 35	53.1	52.7	62.7	61.8
% of patients achieving PASI 90	Week 51	48.8	51.0	60.4	62.9
% of patients achieving PASI 100	Week 35	28.6	30.9	35.3	33.3
% of patients achieving PASI 100	Week 51	25.6	29.6	31.3	35.1

Percentages are calculated based on N', PASI=Psoriasis Area and Severity Index.

The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2 and the Extension Period. Percentages are calculated based on N'

Summary of IGA responders and number of patients with DLQI score 0 or 1 by visit and treatment group - Week 17 (PPS)

	IGA responder, n/N' (%)	
	GP2017	Humira

Visit	N=197	N=196
Week 17	103/192 (53.6)	104/194 (53.6)

	DLQI score 0 or 1, n/N' (%)	
	GP2017	Humira
Visit	N=197	N=196
Week 17	97/192 (50.5)	93/192 (48.4)

Percentages are calculated based on N'.

IGA=Investigator's global assessment; N=number of patients per treatment group; N'=number of patients with evaluable data per treatment group; n=number of patients per treatment group achieving IGA score response (defined as clear [0] or almost clear [1] disease state and improved by at least 2 points of the IGA scale since baseline assessment); PPS=per-protocol analysis set

DLQI=dermatology life quality index; N=number of patients per treatment group; N'=number of patients with evaluable data per treatment group; n=number of patients per treatment group achieving response (DLQI score of 0 or 1); PPS=per-protocol analysis set

Summary of IGA responders and number of patients with DLQI score 0 or 1 by visit and individual group –at Week 35 and Week 51 (TP2+EP PPS)

	IGA responder, n/N' (%)			
	Humira to GP2017	Continued Humira	GP2017 to Humira	Continued GP2017
Visit	N=51	N=115	N=55	N=105
Week 35	29/49 (59.2)	64/110 (58.2)	30/51 (58.8)	60/102 (58.8)
Week 51	20/43 (46.5)	54/98 (55.1)	28/48 (58.3)	58/97 (59.8)
	DLQI score 0 or 1, n/N' (%)			
Visit				
Week 35	24/49 (49.0)	60/110 (54.5)	27/51 (52.9)	57/102 (55.9)
Week 51	21/43 (48.8)	55/99 (55.6)	26/48 (54.2)	58/97 (59.8)

The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2 and the Extension Period. Percentages are calculated based on N'.

IGA=Investigator's global assessment; N=number of patients per treatment group; N'=number of patients with evaluable data per treatment group; n=number of patients per treatment group achieving IGA score response (defined as clear [0] or almost clear [1] disease state and improved by at least 2 points of the IGA scale since baseline assessment); PPS=per-protocol analysis set

DLQI=dermatology life quality index; N=number of patients per treatment group; N'=number of patients with evaluable data per treatment group; n=number of patients per treatment group achieving response (DLQI score of 0 or 1); TP2+EP PPS=per-protocol analysis set during Treatment Period 2 and the Extension Period

Summary of patients with confirmed positive ADA response by treatment group – Overall from Randomization to Week 17 (SAF)

	GP2017 N=231	Humira N=234
ADA response	**n/N' (%)**	**n/N' (%)**
Overall from Week 1[b]		
Positive	81/220 (36.8)	75/220 (34.1)

ADA=anti-drug antibody; n=number of patients per treatment group with ADA response; N=number of patients per treatment group; N'=number of patients with evaluable data; SAF=safety analysis set

[b] 'Overall from Week 1' indicates that patients had at least one ADA positive result (recorded as positive) or had consistently negative results (recorded as negative) post-baseline.

Summary of patients with confirmed positive ADA response by individual group – Overall from Randomization to Week 51 (TP2+EP SAF)

ADA response	Humira to GP2017 N=63 n/N' (%)	Continued Humira N=127 n/N' (%)	GP2017 to Humira N=63 n/N' (%)	Continued GP2017 N=126 n/N' (%)
Overall from Week 1[b]				
Positive	24/61 (39.3)	55/122 (45.1)	28/60 (46.7)	44/123 (35.8)

The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2.

ADA=anti-drug antibody; n=number of patients per treatment group with ADA response; N=number of patients per treatment group; N'=number of patients with evaluable data; TP2+EP SAF=safety analysis set Treatment Period 2 and Extension Period

[b] 'Overall from Week 1' indicates that patients had at least one ADA positive result (recorded as positive) or had consistently negative results (recorded as negative) post-baseline.

Summary of Safety

Safety Results

Serious Adverse Events and Deaths

SAEs regardless of study drug relationship by system organ class and preferred term by treatment group – Randomization to Week 17 (SAF)

System organ class Preferred term	GP2017 N=231 n (%)	Humira N=234 n (%)
Number of patients with at least one SAE	3 (1.3)	10 (4.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (0.9)	3 (1.3)
Basal cell carcinoma	2 (0.9)	2 (0.9)
Prostate cancer	0 (0.0)	1 (0.4)
Infections and infestations	1 (0.4)	2 (0.9)
Staphylococcal infection	1 (0.4)	0 (0.0)
Cellulitis	0 (0.0)	1 (0.4)
Pneumonia	0 (0.0)	1 (0.4)
Immune system disorders	1 (0.4)	0 (0.0)
Hypersensitivity	1 (0.4)	0 (0.0)
Gastrointestinal disorders	0 (0.0)	2 (0.9)
Abdominal pain	0 (0.0)	1 (0.4)
Vomiting	0 (0.0)	1 (0.4)
Pregnancy, puerperium and perinatal conditions	0 (0.0)	1 (0.4)
Ectopic pregnancy	0 (0.0)	1 (0.4)

System organ class Preferred term	GP2017 N=231 n (%)	Humira N=234 n (%)
Renal and urinary disorders	0 (0.0)	1 (0.4)
Renal colic	0 (0.0)	1 (0.4)
Skin and subcutaneous tissue disorders	0 (0.0)	1 (0.4)
Toxic skin eruption [1]	0 (0.0)	1 (0.4)

System organ classes and preferred terms are sorted by decreasing frequency in the GP2017 treatment group.

Percentages are based on the number of patients within the treatment group in the SAF (N). Patients experiencing multiple events within the same preferred term and/or system organ class are counted only once under those categories.

SAF=safety analysis set; SAE=serious adverse event; SUSAR=suspected unexpected serious adverse reaction

[1] Reported as SUSAR to the competent authorities and IECs/IRBs as required

SAEs regardless of study drug relationship by system organ class and preferred term by individual group – Week 17 to Week 51 (TP2+EP SAF)

System organ class Preferred term	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Number of patients with at least one SAE	4 (6.3)	8 (6.3)	2 (3.2)	3 (2.4)
General disorders and administration site conditions	2 (3.2)	1 (0.8)	0 (0.0)	0 (0.0)
Non-cardiac chest pain	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Pyrexia	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Chest pain	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Infections and infestations	1 (1.6)	3 (2.4)	0 (0.0)	1 (0.8)
Pneumonia	1 (1.6)	1 (0.8)	0 (0.0)	0 (0.0)

System organ class Preferred term	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Pneumonia necrotising	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Pulmonary tuberculosis	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Pyelonephritis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Sepsis	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Renal and urinary disorders	1 (1.6)	1 (0.8)	0 (0.0)	0 (0.0)
Renal colic	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Renal haematoma	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Joint effusion	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0)	2 (1.6)	1 (1.6)	0 (0.0)
Adenocarcinoma of colon	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Chronic lymphocytic leukaemia	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Prostate cancer	0 (0.0)	0 (0.0)	1 (1.6)	0 (0.0)
Psychiatric disorders	0 (0.0)	1 (0.8)	1 (1.6)	1 (0.8)
Completed suicide	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Schizoaffective disorder	0 (0.0)	0 (0.0)	1 (1.6)	0 (0.0)
Suicide attempt	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Cardiac disorders	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)
Cardiomyopathy	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Coronary artery disease	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Abdominal pain	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Oropharyngeal pain	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)

	Humira to GP2017	Continued Humira	GP2017 to Humira	Continued GP2017
System organ class	**N=63**	**N=127**	**N=63**	**N=126**
Preferred term	**n (%)**	**n (%)**	**n (%)**	**n (%)**

System organ classes and preferred terms are sorted by decreasing frequency in the Humira to GP2017 group. The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2.

Percentages are based on the number of patients within the treatment group in the TP2+EP SAF (N). Patients experiencing multiple events within the same preferred term and/or system organ class are counted only once under those categories.

SAE=serious adverse event; TP2+EP SAF=safety analysis set Treatment Period 2 and Extension Period

AEs regardless of study treatment relationship by system organ class and preferred term (at least 2% of patients in any treatment group) by treatment group – Randomization to Week 17 (SAF)

	GP2017	Humira
System organ class	**N=231**	**N=234**
Preferred term	**n (%)**	**n (%)**
Number of patients with at least one AE	116 (50.2)	123 (52.6)
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)

System organ class Preferred term	GP2017 N=231 n (%)	Humira N=234 n (%)
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)
Diarrhoea	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 (incl cysts and polyps)	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)

System organ classes and preferred terms are sorted by decreasing frequency in the GP2017 treatment group.

Percentages are based on the number of patients within the treatment group in the SAF (N). Patients experiencing multiple events within the same preferred term and/or system organ class are counted only once under those categories.

AE=adverse event; SAF=safety analysis set

AEs regardless of study treatment relationship by system organ class and preferred term (at least 3% of patients in any treatment group) by individual group - Week 17 to Week 51 (TP2+EP SAF)

System organ class Preferred term	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Number of patients with at least one AE	29 (46.0)	71 (55.9)	36 (57.1)	66 (52.4)
Infections and infestations	17 (27.0)	34 (26.8)	21 (33.3)	39 (31.0)
Upper respiratory tract infection	4 (6.3)	6 (4.7)	0 (0.0)	6 (4.8)
Bronchitis	3 (4.8)	1 (0.8)	2 (3.2)	5 (4.0)
Nasopharyngitis	2 (3.2)	8 (6.3)	6 (9.5)	9 (7.1)
Viral upper respiratory tract infection	2 (3.2)	1 (0.8)	1 (1.6)	2 (1.6)
Sinusitis	1 (1.6)	3 (2.4)	2 (3.2)	6 (4.8)
Gastroenteritis viral	1 (1.6)	2 (1.6)	2 (3.2)	1 (0.8)
Influenza	1 (1.6)	1 (0.8)	2 (3.2)	0 (0.0)
Staphylococcal infection	1 (1.6)	1 (0.8)	2 (3.2)	0 (0.0)
Skin and subcutaneous tissue disorders	8 (12.7)	9 (7.1)	3 (4.8)	11 (8.7)
Dry skin	2 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)
Psoriasis	2 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)
Urticaria	2 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis contact	0 (0.0)	1 (0.8)	1 (1.6)	4 (3.2)
General disorders and administration site conditions	7 (11.1)	13 (10.2)	5 (7.9)	10 (7.9)
Non-cardiac chest pain	2 (3.2)	0 (0.0)	0 (0.0)	2 (1.6)
Injection site erythema	0 (0.0)	2 (1.6)	2 (3.2)	4 (3.2)
Respiratory, thoracic and mediastinal disorders	6 (9.5)	10 (7.9)	4 (6.3)	4 (3.2)
Cough	3 (4.8)	3 (2.4)	0 (0.0)	1 (0.8)
Injury, poisoning and procedural complications	6 (9.5)	8 (6.3)	2 (3.2)	5 (4.0)
Muscle strain	3 (4.8)	1 (0.8)	1 (1.6)	1 (0.8)

System organ class Preferred term	Humira to GP2017 N=63 n (%)	Continued Humira N=127 n (%)	GP2017 to Humira N=63 n (%)	Continued GP2017 N=126 n (%)
Musculoskeletal and connective tissue disorders	5 (7.9)	11 (8.7)	8 (12.7)	12 (9.5)
Arthralgia	1 (1.6)	3 (2.4)	3 (4.8)	4 (3.2)
Back pain	1 (1.6)	3 (2.4)	3 (4.8)	2 (1.6)
Pain in extremity	0 (0.0)	1 (0.8)	2 (3.2)	0 (0.0)
Nervous system disorders	5 (7.9)	8 (6.3)	3 (4.8)	10 (7.9)
Headache	5 (7.9)	2 (1.6)	2 (3.2)	6 (4.8)
Gastrointestinal disorders	2 (3.2)	18 (14.2)	4 (6.3)	8 (6.3)
Nausea	1 (1.6)	4 (3.1)	1 (1.6)	1 (0.8)
Constipation	1 (1.6)	4 (3.1)	0 (0.0)	1 (0.8)
Investigations	2 (3.2)	12 (9.4)	6 (9.5)	5 (4.0)
Alanine aminotransferase increased	0 (0.0)	2 (1.6)	2 (3.2)	0 (0.0)
Gamma-glutamyltransferase increased	0 (0.0)	0 (0.0)	3 (4.8)	0 (0.0)
Aspartate aminotransferase increased	0 (0.0)	0 (0.0)	2 (3.2)	0 (0.0)
Psychiatric disorders	2 (3.2)	5 (3.9)	2 (3.2)	4 (3.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (3.2)	3 (2.4)	2 (3.2)	0 (0.0)
Renal and urinary disorders	2 (3.2)	3 (2.4)	0 (0.0)	0 (0.0)
Vascular disorders	1 (1.6)	7 (5.5)	0 (0.0)	2 (1.6)
Hypertension	1 (1.6)	7 (5.5)	0 (0.0)	2 (1.6)
Blood and lymphatic system disorders	1 (1.6)	2 (1.6)	3 (4.8)	3 (2.4)
Thrombocytopenia	0 (0.0)	1 (0.8)	2 (3.2)	0 (0.0)
Immune system disorders	1 (1.6)	4 (3.1)	0 (0.0)	4 (3.2)
Seasonal allergy	1 (1.6)	3 (2.4)	0 (0.0)	4 (3.2)
Metabolism and nutrition disorders	1 (1.6)	0 (0.0)	2 (3.2)	2 (1.6)
Eye disorders	0 (0.0)	1 (0.8)	4 (6.3)	4 (3.2)

	Humira to GP2017	Continued Humira	GP2017 to Humira	Continued GP2017
System organ class	**N=63**	**N=127**	**N=63**	**N=126**
Preferred term	**n (%)**	**n (%)**	**n (%)**	**n (%)**

System organ classes and preferred terms are sorted by decreasing frequency in the Humira to GP2017 group. The continued groups include patients who continued the same treatment throughout the study; the switched groups include patients who switched treatment between GP2017 and Humira during Treatment Period 2.

Percentages are based on the number of patients within the treatment group in the TP2+EP SAF (N). Patients experiencing multiple events within the same preferred term and/or system organ class are counted only once under those categories.

AE=adverse event; TP2+EP SAF=safety analysis set Treatment Period 2 and Extension Period

Other Relevant Findings

N/A

Conclusion:

The results of this study demonstrated equivalent efficacy of GP2017 and Humira in patients with moderate to severe chronic plaque-type psoriasis. Efficacy was sustained and similar across groups up to the end of the study at Week 51. No clinically relevant differences in efficacy between patients continuously treated with GP2017 or Humira as compared to patients who repeatedly switched between GP2017 and Humira were observed. Safety profiles and immunogenicity were generally similar among patients treated with GP2017 and Humira and patients undergoing repeated treatment switches. No clinically relevant differences between patients continuously treated with GP2017 and patients continuously treated with Humira and between patients continuously treated with GP2017 or Humira and patients who repeatedly switched treatments were observed in terms of long-term safety and immunogenicity. To conclude, the data obtained in this study are well in line with knowledge on adalimumab used to treat psoriasis.

Date of Clinical Trial Report

7 March 2017