Clinical trial results:
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

Summary

EudraCT number	2013-000747-11
Trial protocol	BG SK PL
Global end of trial date	25 February 2016

Results information

Result version number	v1 (current)
This version publication date	10 March 2017
First version publication date	10 March 2017

Trial information

Trial identification

Sponsor protocol code	GP17-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02016105
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hexal AG
Sponsor organisation address	Industriestrasse 25, Holzkirchen, Germany, 83607
Public contact	Strategic Planning Biopharma Clinical Development, Sandoz, 0049 80244760, biopharma.clinicaltrials@sandoz.com
Scientific contact	Strategic Planning Biopharma Clinical Development, Sandoz, 0049 80244760, biopharma.clinicaltrials@sandoz.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2015
Global end of trial reached?	Yes
Global end of trial date	25 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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 PASI75 response rate at Week 16.

Protection of trial subjects:

This trial was designed, conducted and reported in accordance with the international Conference on Harmonization (ICH) Guidelines for Good Clinical Practice (GCP), applicable local regulations (including European Directive 2001/20/EC), and following the ethical principles laid down in the Declaration of Helsinki. Specific ICH adopted and other relevant international guidelines and recommendations were taken into account as far as meaningfully possible. Safety assessments included adverse events (AEs), vital signs, 12-lead ECG parameters, clinical laboratory, immunogenicity, physical examination and other parameters considered relevant for the safety assessment, of Adalumimab.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Slovakia: 31
Country: Number of subjects enrolled	Bulgaria: 31
Country: Number of subjects enrolled	United States: 378
Worldwide total number of subjects	465
EEA total number of subjects	87

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	413
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

661 patients were screened. 465 patients were randomized 1:1 into Treatment Period 1 and stratified by region (US/EU), body weight (<90/≥90 kg) and prior systemic therapy (no/any). In Treatment Period 2 patients were re-randomized 2:1 to either continue orginally assigned treatment or switch treatment and were stratified by region only.

Pre-assignment

Screening details:

Screening lasted for at least 2 weeks and up to 4 weeks. Main inclusion criteria:
- Men or women of at least 18 years
- Chronic plaque-type psoriasis ≥ 6 months before randomization
- Moderate to severe psoriasis :
->PASI score ≥ 12
-> IGA score ≥3
-> BSA affected by plaque-type psoriasis ≥ 10%
- No previous exposure to adalimumab

Period 1

Period 1 title	Treatment period 1 (Day 1-Week 17)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Patients were asked not to look at the syringes during administration. To maintain the blind of the assessing investigator, independent, unblinded site personnel handled and administered the treatment. Patients, investigator staff, and persons performing the assessments remained blinded to the identity of the treatment until the database lock (Week 51 analysis). After database-lock for the primary analysis only designated sponsor data analysts were unblinded to perfom the Week 17 analysis.

Arms

Are arms mutually exclusive?	Yes
Arm title	GP2017

Arm description:

GP2017 subcutaneous injections

Arm type	Experimental
Investigational medicinal product name	GP2017
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The proposed biosimilar GP2017 was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection at a loading dose of 80 mg at Day 1, and subsequent doses of 40 mg eow, starting one week after the loading dose.

Arm title	Humira

Arm description:

Humira subcutaneous injections

Arm type	Active comparator

Investigational medicinal product name	Humira
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira (US Humira in the US and EU Humira in the EU) was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection at a loading dose of 80 mg at Day 1, and subsequent doses of 40 mg eow, starting one week after the loading dose.

Number of subjects in period 1	GP2017	Humira
Started	231	234
Completed	201	201
Not completed	30	33
Consent withdrawn by subject	15	11
Physician decision	-	2
Adverse event, non-fatal	3	5
Pregnancy	-	1
Lost to follow-up	6	4
Protocol deviation	2	8
Lack of efficacy	4	2

Period 2

Period 2 title	Treatment period 2 (Week 17-35)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The blinding details were continued as described in Treatment period 1.

Arms

Are arms mutually exclusive?	Yes
Arm title	Humira continued

Arm description:

Humira subcutaneous injections, continued treatment

Arm type	Active comparator

Investigational medicinal product name	Humira
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira ((US Humira in the US and EU Humira in the EU) was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	GP2017 continued

Arm description:

GP2017 subcutaneous injections, continued treatment

Arm type	Experimental
Investigational medicinal product name	GP2017
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The proposed biosimilar GP2017 was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	Humira switched

Arm description:

Subcutaneous injections switching: Patients started with Humira treatment in Treatment period 1 switched to s.c. injections with GP2017, 40 mg eow betweem Week 17 to Week 23; then switched to s.c. injections with Humira, 40 mg eow between Week 23 to Week 29; and again switched to s.c. injections with GP2017, 40 mg eow from Week 29 to Week 35.

Arm type	Experimental/Active comparator
Investigational medicinal product name	GP2017 & Humira
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The proposed biosimilar GP2017 and Humira (US Humira in the US and EU Humira in the EU) was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	GP2017 switched

Arm description:

Subcutaneous injections switching: Patients started with GP2017 treatment in Treatment period 1 switched to s.c. injections with Humira, 40 mg eow between Week 17 to Week 23; then switched to s.c. injections with GP2017, 40 mg eow between Week 23 to Week 29; and again switched to s.c. injections with Humira, 40 mg eow between Week 29 to Week 35.

Arm type	Experimental/Active comparator
Investigational medicinal product name	Humira & GP2017
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira (US Humira in the US and EU Humira in the EU) and the proposed biosimilar GP2017 was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Number of subjects in period 2[1]	Humira continued	GP2017 continued	Humira switched
Started	127	126	63
Completed	116	112	57
Not completed	11	14	6
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	7	3
Non compliance Study Medication	-	1	-
Adverse event, non-fatal	4	1	-
Pregnancy	-	1	-
Lost to follow-up	-	1	1
Lack of efficacy	6	2	2

Number of subjects in period 2[1]	GP2017 switched
Started	63
Completed	59
Not completed	4
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Non compliance Study Medication	-
Adverse event, non-fatal	-
Pregnancy	-
Lost to follow-up	-
Lack of efficacy	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only subject eligible to proceed to Treatment Period 2 were analyzed as per protocol.

Period 3

Period 3 title	Extension period (Week 35-51)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The blinding details were continued as described in Treatment period 1.

Arms

Are arms mutually exclusive?	Yes

Arm title	Humira continued Extension period

Arm description:

Continued Humira treatment from Treatment Period 1 and 2 into Extension period.

Arm type	Active comparator
Investigational medicinal product name	Humira
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira (US Humira in the US and EU Humira in the EU) was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	GP2017 continued Extension period

Arm description:

Continued GP2017 treatment from Treatment Period 1 and 2 into Extension period.

Arm type	Experimental
Investigational medicinal product name	GP2017
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The proposed biosimilar GP2017 was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	Humira switched Extension period

Arm description:

At the end of Treatment Period 2, patients continued in the study for an additional 16 weeks during the Extension Period up to week 51 and received the same treatment they received during Treatment Period 1. No further switches were performed.

Arm type	Experimental/Active comparator
Investigational medicinal product name	Humira
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira (US Humira in the US and EU Humira in the EU) was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Arm title	GP2017 switched Extension period

Arm description:

At the end of Treatment Period 2, patients continued in the study for an additional 16 weeks during the Extension Period up to week 51 and received the same treatment they received during Treatment Period 1. No further switches were performed.

Arm type	Experimental/Active comparator
Investigational medicinal product name	GP2017
Investigational medicinal product code	adalimumab
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The proposed biosimilar GP2017 was supplied to the investigators in prefilled syringes containing 40 mg of the active ingredient in a 0.8 mL solution. All study treatments were administered by s.c. injection, and subsequent doses of 40 mg eow.

Number of subjects in period 3[2]	Humira continued Extension period	GP2017 continued Extension period	Humira switched Extension period
Started	109	106	52
Completed	104	100	47
Not completed	5	6	5
Consent withdrawn by subject	2	2	2
Adverse event, non-fatal	-	-	2
Non Compliance with Study Medication	-	-	-
Lost to follow-up	-	2	-
New Therapy for study indication	-	1	-
Lack of efficacy	3	1	1

Number of subjects in period 3[2]	GP2017 switched Extension period
Started	56
Completed	50
Not completed	6
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Non Compliance with Study Medication	1
Lost to follow-up	-
New Therapy for study indication	1
Lack of efficacy	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: In the extention period, subject set analyzed was the analysis set Treatment Period 2 plus Extension Period as per SAP.

Baseline characteristics

Reporting groups	
Reporting group title	GP2017
Reporting group description: GP2017 subcutaneous injections	
Reporting group title	Humira
Reporting group description: Humira subcutaneous injections	

Reporting group values	GP2017	Humira	Total
Number of subjects	231	234	465
Age categorical Units: Subjects			
Adults (18-64 years)	205	208	413
Adults (65-84 years)	26	26	52
Age continuous Units: years			
arithmetic mean	45.6	46.9	
standard deviation	± 14.16	± 14.09	-
Gender categorical Units: Subjects			
Female	89	92	181
Male	142	142	284
Race Units: Subjects			
Caucasian	196	201	397
Black	14	9	23
Asian	3	5	8
Native American	4	4	8
Pacific Islander	0	1	1
Other	11	14	25
Unknown	3	0	3
Weight Units: kg			
arithmetic mean	92.76	90.95	
standard deviation	± 26.267	± 24.231	-
BMI Units: kg/m2			
arithmetic mean	31.41	30.72	
standard deviation	± 8.122	± 7.484	-

End points

End points reporting groups

Reporting group title	GP2017
Reporting group description: GP2017 subcutaneous injections	
Reporting group title	Humira
Reporting group description: Humira subcutaneous injections	
Reporting group title	Humira continued
Reporting group description: Humira subcutaneous injections, continued treatment	
Reporting group title	GP2017 continued
Reporting group description: GP2017 subcutaneous injections, continued treatment	
Reporting group title	Humira switched
Reporting group description: Subcutaneous injections switching: Patients started with Humira treatment in Treatment period 1 switched to s.c. injections with GP2017, 40 mg eow betweem Week 17 to Week 23; then switched to s.c. injections with Humira, 40 mg eow between Week 23 to Week 29; and again switched to s.c. injections with GP2017, 40 mg eow from Week 29 to Week 35.	
Reporting group title	GP2017 switched
Reporting group description: Subcutaneous injections switching: Patients started with GP2017 treatment in Treatment period 1 switched to s.c. injections with Humira, 40 mg eow between Week 17 to Week 23; then switched to s.c. injections with GP2017, 40 mg eow between Week 23 to Week 29; and again switched to s.c. injections with Humira, 40 mg eow between Week 29 to Week 35.	
Reporting group title	Humira continued Extension period
Reporting group description: Continued Humira treatment from Treatment Period 1 and 2 into Extension period.	
Reporting group title	GP2017 continued Extension period
Reporting group description: Continued GP2017 treatment from Treatment Period 1 and 2 into Extension period.	
Reporting group title	Humira switched Extension period
Reporting group description: At the end of Treatment Period 2, patients continued in the study for an additional 16 weeks during the Extension Period up to week 51 and received the same treatment they received during Treatment Period 1. No further switches were performed.	
Reporting group title	GP2017 switched Extension period
Reporting group description: At the end of Treatment Period 2, patients continued in the study for an additional 16 weeks during the Extension Period up to week 51 and received the same treatment they received during Treatment Period 1. No further switches were performed.	
Subject analysis set title	Population for Immunogenicity Analysis GP2017 Adalimumab
Subject analysis set type	Safety analysis
Subject analysis set description: Population for Treatment Period 1 (Immunogenicity Analysis) for GP2017 Adalimumab	
Subject analysis set title	Population Immunogenicity Analysis Humira®Adalimumab continued
Subject analysis set type	Safety analysis
Subject analysis set description: Population from Randomization to Week 51 (Immunogenicity Analysis) for Humira®Adalimumab continued	
Subject analysis set title	Population for Immunogenicity Analysis Humira®Adalimumb

Subject analysis set type	Safety analysis
Subject analysis set description:	
Population for Treatment Period 1 (Immunogenicity Analysis) for Humira®Adalimumab	
Subject analysis set title	Population Immunogenicity Analysis GP2017 Adalimumab continued
Subject analysis set type	Safety analysis
Subject analysis set description:	
Population from Randomization to Week 51 (Immunogenicity Analysis) for GP2017 Adalimumab continued	
Subject analysis set title	Population Immunogenicity Analysis GP2017 Adalimumab switched
Subject analysis set type	Safety analysis
Subject analysis set description:	
Population from Randomization to Week 51 (Immunogenicity Analysis) for GP2017 Adalimumab switched	
Subject analysis set title	Population Immunogenicity Analysis Humira® Adalimumab switched
Subject analysis set type	Safety analysis
Subject analysis set description:	
Population from Randomization to Week 51 (Immunogenicity Analysis) for Humira® Adalimumab switched	

Primary: PASI75 response rate at Week 16

End point title	PASI75 response rate at Week 16
End point description:	
The primary variable was the PASI75 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 with baseline.	
End point type	Primary
End point timeframe:	
Week 16	

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197[1]	196[2]		
Units: percent				
number (not applicable)	66.8	65		

Notes:

[1] - Per Protocol Set

[2] - Per Protocol Set

Statistical analyses

Statistical analysis title	Logistic regression GP2017 v Humira
Statistical analysis description:	
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. To conclude equivalent efficacy, the 95% CI had to be entirely within the interval [-18%, 18%].	
Comparison groups	GP2017 v Humira

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	equivalence
Method	Regression, Logistic
Parameter estimate	95% of Response Rate Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.46
upper limit	11.15

Secondary: Mean percent change from baseline in PASI score up to Week 16 (MMRM)

End point title	Mean percent change from baseline in PASI score up to Week 16 (MMRM)

End point description:

Key Secondary: Percentage change from baseline in PASI score at each visit up to Week 16

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197[3]	196[4]		
Units: percent				
number (not applicable)	-60.7	-61.5		

Notes:

[3] - Per Protocol Set

[4] - Per Protocol Set

Statistical analyses

Statistical analysis title	Mixed model repeated measures (MMRM)

Statistical analysis description:

LSM, SE and 95% CI were estimated by a Mixed Model 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. Therapeutic equivalence in terms of the % change from baseline in PASI score was to be determined if the 95% CI for the difference between GP2015 and Humira was contained within the interval [−15%, 15%].

Comparison groups	GP2017 v Humira
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	equivalence
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.15
upper limit	4.84

Secondary: Mean ATE of percent change from baseline in PASI score

End point title	Mean ATE of percent change from baseline in PASI score

End point description:

Key Secondary: Average Treatment Effect (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).

End point type	Secondary

End point timeframe:

Week 1 to Week 16

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197[5]	196[6]		
Units: percent				
number (not applicable)	-59.7	-60.8		

Notes:

[5] - Per Protocol Set

[6] - Per Protocol Set

Statistical analyses

Statistical analysis title	ANCOVA of Average Treatment Effect (ATE)

Statistical analysis description:

LSM, 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. Therapeutic equivalence in terms of the % change from baseline in PASI score was to be determined if the 95% CI for the difference between GP2017 and Humira was contained within the interval [−15%, 15%].

Comparison groups	GP2017 v Humira
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	equivalence
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.78
upper limit	5.08

Secondary: PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 17

End point title	PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 17

End point description:

To compare PASI50, PASI75, PASI90 and PASI100 response rates of patients treated with GP2017 and Humira at Week 17

End point type	Secondary

End point timeframe:

End of Treatment Period 1 (Week 17)

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	196		
Units: percent				
number (not applicable)				
PASI 50	93.2	92.8		
PASI 75	71.4	68.6		
PASI 90	51.6	44.8		
PASI100	21.9	16.5		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 35

End point title	PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 35

End point description:

To compare PASI50, PASI75, PASI90 and PASI100 response rates of patients treated with GP2017 and Humira at Week 35

End point type	Secondary

End point timeframe:

End of Treatment Period 2 (Week 35)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)				
PASI50	96.4	96.1	95.9	94.1

PASI75	73.6	74.5	73.5	70.6
PASI90	52.7	61.8	53.1	62.7
PASI100	30.9	33.3	28.6	35.3

Statistical analyses

No statistical analyses for this end point

Secondary: PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 51

End point title	PASI50, PASI75, PASI90 and PASI100 Response Rate at Week 51

End point description:

To compare PASI50, PASI75, PASI90 and PASI100 response rates of patients treated with GP2017 and Humira at Week 51

End point type	Secondary

End point timeframe:

End of Extension Period (Week 51)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)				
PASI 50	93.9	95.9	95.3	87.5
PASI 75	79.6	84.5	76.7	75
PASI 90	51	62.9	48.8	60.4
PASI 100	29.6	35.1	25.6	31.3

Statistical analyses

No statistical analyses for this end point

Secondary: IGA Response Rate at Week 17

End point title	IGA Response Rate at Week 17

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 17 compared to baseline

End point type	Secondary

End point timeframe:

End of Treatment Period 1 (Week 17)

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	196		
Units: percent				
number (not applicable)	53.6	53.6		

Statistical analyses

No statistical analyses for this end point

Secondary: IGA Response Rate at Week 35

End point title	IGA Response Rate at Week 35

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 35 compared to baseline

End point type	Secondary

End point timeframe:

End of Treatment Period 2 (Week 35)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)	58.2	58.8	59.2	58.8

Statistical analyses

No statistical analyses for this end point

Secondary: IGA Response Rate at Week 51

End point title	IGA Response Rate at Week 51

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 51 compared to baseline

End point type	Secondary

End point timeframe:

End of Extension Period (Week 51)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)	55.1	59.8	46.5	58.3

Statistical analyses

No statistical analyses for this end point

Secondary: DLQI at Week 17

End point title	DLQI at Week 17

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 17 compared to baseline

End point type	Secondary

End point timeframe:

End of Treatment Period 1 (Week 17)

End point values	GP2017	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	196		
Units: percent				
number (not applicable)	50.5	48.4		

Statistical analyses

No statistical analyses for this end point

Secondary: DLQI at Week 35

End point title	DLQI at Week 35

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 35 compared to baseline

End point type	Secondary

End point timeframe:

End of Treatment Period 2 (Week 35)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)	54.5	55.9	49	52.9

Statistical analyses

No statistical analyses for this end point

Secondary: DLQI at Week 51

End point title	DLQI at Week 51

End point description:

Proportion of patients achieving a score of 0 ("Clear") or 1 ("almost clear") or improved by at least 2 pointsof the IGA scale at Week 51 compared to baseline

End point type	Secondary

End point timeframe:

End of Extension Period (Week 51)

End point values	Humira continued	GP2017 continued	Humira switched	GP2017 switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	105	51	55
Units: percent				
number (not applicable)	55.6	59.8	48.8	54.2

Statistical analyses

No statistical analyses for this end point

Secondary: ADA formation against GP2017 adalimumab and Humira® adalimumab from Randomization until Week 17

End point title	ADA formation against GP2017 adalimumab and Humira® adalimumab from Randomization until Week 17

End point description:

Proportion of patients with at least one confirmed positive anti-drug antibodies (ADA) response to adalimumab from Randomization to Week 17.
Patients with ADA positive results at baseline were excluded from subsequent results.

End point type	Secondary

End point timeframe:

Randomization to Week 17 (Treatment Period 1)

End point values	Population for Immunogenicity Analysis GP2017 Adalimumab	Population for Immunogenicity Analysis Humira®Adalimumb		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	231	234		
Units: percent				
number (not applicable)	36.8	34.1		

Statistical analyses

No statistical analyses for this end point

Secondary: ADA formation against GP2017 adalimumab and Humira® adalimumab from Randomization to Week 51

End point title	ADA formation against GP2017 adalimumab and Humira® adalimumab from Randomization to Week 51

End point description:

Patients with ADA positive results at baseline were excluded from subsequent results.

End point type	Secondary

End point timeframe:

Randomization until Week 51 (Treatment Period 1 and Treatment Period 2 and Extension Period)

End point values	Population Immunogenicity Analysis Humira®Adalimumab continued	Population Immunogenicity Analysis GP2017 Adalimumab continued	Population Immunogenicity Analysis GP2017 Adalimumab switched	Population Immunogenicity Analysis Humira® Adalimumab switched
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	127	126	63	63
Units: percent				
number (not applicable)	45.1	35.8	46.7	39.3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs are reported from date patient has provided informed consent and until 30 days after the patient has stopped study participation. AEs are analyzed from start date of study treatment to date of study completion/early discontinuation.

Adverse event reporting additional description:

The occurrence of AEs should be sought by non-directive questioning of the patient at each visit during the study. AEs also may be detected when they are volunteered by the patient during or between visits or through physical examination, laboratory test, or other assessments.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Humira continued

Reporting group description:

In this reporting group data from Treatment Period 1, Treatment Period 2 and Extension Period is combined to reflect the entire study.

Reporting group title	Humira switched

Reporting group description:

In this reporting group data from Treatment Period 1, Treatment Period 2 and Extension Period is combined to reflect the entire study.

Reporting group title	GP2017 switched

Reporting group description:

In this reporting group data from Treatment Period 1, Treatment Period 2 and Extension Period is combined to reflect the entire study.

Reporting group title	GP2017 continued

Reporting group description:

In this reporting group data from Treatment Period 1, Treatment Period 2 and Extension Period is combined to reflect the entire study.

Serious adverse events	Humira continued	Humira switched	GP2017 switched
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 127 (7.87%)	6 / 63 (9.52%)	2 / 63 (3.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 127 (0.79%)	1 / 63 (1.59%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			

subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non cardiac chest pain			
subjects affected / exposed	0 / 127 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Swelling			
subjects affected / exposed	0 / 127 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizoaffective disorder			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			

subjects affected / exposed	0 / 127 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haematoma			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 127 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 127 (0.79%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GP2017 continued		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 126 (3.17%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non cardiac chest pain			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Swelling			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Schizoaffective disorder			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal haematoma			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia necrotising			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary tuberculosis			

subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Humira continued	Humira switched	GP2017 switched
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 127 (66.93%)	40 / 63 (63.49%)	47 / 63 (74.60%)
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 127 (7.87%)	3 / 63 (4.76%)	0 / 63 (0.00%)
occurrences (all)	10	3	0
Total - Vascular disorders			
subjects affected / exposed	12 / 127 (9.45%)	3 / 63 (4.76%)	1 / 63 (1.59%)
occurrences (all)	14	3	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	3 / 127 (2.36%)	0 / 63 (0.00%)	5 / 63 (7.94%)
occurrences (all)	3	0	14
Injection site bruising			
subjects affected / exposed	3 / 127 (2.36%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	3	2	0
Injection site pain			
subjects affected / exposed	2 / 127 (1.57%)	1 / 63 (1.59%)	2 / 63 (3.17%)
occurrences (all)	2	1	15
Injection site pruritus			

subjects affected / exposed	1 / 127 (0.79%)	1 / 63 (1.59%)	2 / 63 (3.17%)
occurrences (all)	2	1	2
Injection site induration			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	7 / 127 (5.51%)	1 / 63 (1.59%)	4 / 63 (6.35%)
occurrences (all)	8	1	5
Total - General disorders and administration site conditions			
subjects affected / exposed	17 / 127 (13.39%)	9 / 63 (14.29%)	12 / 63 (19.05%)
occurrences (all)	32	11	49
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	5 / 127 (3.94%)	1 / 63 (1.59%)	1 / 63 (1.59%)
occurrences (all)	5	2	1
Total - Immune system disorders			
subjects affected / exposed	7 / 127 (5.51%)	1 / 63 (1.59%)	1 / 63 (1.59%)
occurrences (all)	7	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 127 (3.94%)	4 / 63 (6.35%)	1 / 63 (1.59%)
occurrences (all)	5	4	1
Oropharyngeal pain			
subjects affected / exposed	3 / 127 (2.36%)	3 / 63 (4.76%)	1 / 63 (1.59%)
occurrences (all)	3	3	1
Sinus congestion			
subjects affected / exposed	4 / 127 (3.15%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	4	0	2
Rhinitis allergic			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	1	0	2
Total - Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	17 / 127 (13.39%)	9 / 63 (14.29%)	6 / 63 (9.52%)
occurrences (all)	22	11	8
Psychiatric disorders			

Anxiety			
subjects affected / exposed	3 / 127 (2.36%)	1 / 63 (1.59%)	3 / 63 (4.76%)
occurrences (all)	3	1	3
Insomnia			
subjects affected / exposed	4 / 127 (3.15%)	1 / 63 (1.59%)	1 / 63 (1.59%)
occurrences (all)	4	1	1
Total - Psychiatric disorders			
subjects affected / exposed	10 / 127 (7.87%)	2 / 63 (3.17%)	3 / 63 (4.76%)
occurrences (all)	12	3	5
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 127 (1.57%)	0 / 63 (0.00%)	4 / 63 (6.35%)
occurrences (all)	2	0	4
Alanine aminotransferase increased			
subjects affected / exposed	2 / 127 (1.57%)	0 / 63 (0.00%)	3 / 63 (4.76%)
occurrences (all)	2	0	3
Weight decreased			
subjects affected / exposed	1 / 127 (0.79%)	1 / 63 (1.59%)	2 / 63 (3.17%)
occurrences (all)	1	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	3 / 63 (4.76%)
occurrences (all)	0	0	3
Total - Investigations			
subjects affected / exposed	17 / 127 (13.39%)	4 / 63 (6.35%)	8 / 63 (12.70%)
occurrences (all)	19	5	15
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	1 / 127 (0.79%)	3 / 63 (4.76%)	1 / 63 (1.59%)
occurrences (all)	1	3	1
Ligament sprain			
subjects affected / exposed	2 / 127 (1.57%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	2	2	0
Total - Injury, poisoning and procedural complications			

subjects affected / exposed	14 / 127 (11.02%)	8 / 63 (12.70%)	3 / 63 (4.76%)
occurrences (all)	18	10	3
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 127 (5.51%)	7 / 63 (11.11%)	2 / 63 (3.17%)
occurrences (all)	8	7	2
Dizziness			
subjects affected / exposed	4 / 127 (3.15%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences (all)	4	0	0
Sciatica			
subjects affected / exposed	0 / 127 (0.00%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Total - Nervous system disorders			
subjects affected / exposed	13 / 127 (10.24%)	10 / 63 (15.87%)	4 / 63 (6.35%)
occurrences (all)	19	11	4
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 127 (2.36%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	5	0	2
Neutropenia			
subjects affected / exposed	1 / 127 (0.79%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	1	2	0
Total - Blood and lymphatic system disorders			
subjects affected / exposed	6 / 127 (4.72%)	2 / 63 (3.17%)	3 / 63 (4.76%)
occurrences (all)	8	3	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 127 (5.51%)	2 / 63 (3.17%)	2 / 63 (3.17%)
occurrences (all)	7	2	2
Toothache			
subjects affected / exposed	4 / 127 (3.15%)	0 / 63 (0.00%)	3 / 63 (4.76%)
occurrences (all)	5	0	3
Nausea			
subjects affected / exposed	4 / 127 (3.15%)	2 / 63 (3.17%)	1 / 63 (1.59%)
occurrences (all)	5	3	1
Dental caries			

subjects affected / exposed	5 / 127 (3.94%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences (all)	5	0	0
Constipation			
subjects affected / exposed	4 / 127 (3.15%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences (all)	6	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 127 (3.15%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences (all)	4	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 127 (0.00%)	2 / 63 (3.17%)	1 / 63 (1.59%)
occurrences (all)	0	2	1
Food poisoning			
subjects affected / exposed	0 / 127 (0.00%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	0	0	3
Total - Gastrointestinal disorders			
subjects affected / exposed	25 / 127 (19.69%)	7 / 63 (11.11%)	9 / 63 (14.29%)
occurrences (all)	46	14	11
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 127 (0.79%)	0 / 63 (0.00%)	2 / 63 (3.17%)
occurrences (all)	1	0	3
Pruritus generalised			
subjects affected / exposed	4 / 127 (3.15%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences (all)	4	1	0
Urticaria			
subjects affected / exposed	2 / 127 (1.57%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	2	2	0
Dermal cyst			
subjects affected / exposed	0 / 127 (0.00%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	0 / 127 (0.00%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Psoriasis			
subjects affected / exposed	0 / 127 (0.00%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	0	2	0

Total - Skin and subcutaneous tissue disorders			
subjects affected / exposed	15 / 127 (11.81%)	8 / 63 (12.70%)	5 / 63 (7.94%)
occurrences (all)	18	14	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 127 (2.36%)	3 / 63 (4.76%)	6 / 63 (9.52%)
occurrences (all)	4	4	6
Back pain			
subjects affected / exposed	5 / 127 (3.94%)	1 / 63 (1.59%)	4 / 63 (6.35%)
occurrences (all)	6	1	4
Pain in extremity			
subjects affected / exposed	2 / 127 (1.57%)	1 / 63 (1.59%)	3 / 63 (4.76%)
occurrences (all)	2	1	4
Musculoskeletal pain			
subjects affected / exposed	1 / 127 (0.79%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	1	2	0
Total - Musculoskeletal and connective tissue disorders			
subjects affected / exposed	18 / 127 (14.17%)	8 / 63 (12.70%)	15 / 63 (23.81%)
occurrences (all)	22	13	21
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	16 / 127 (12.60%)	7 / 63 (11.11%)	8 / 63 (12.70%)
occurrences (all)	17	7	12
Upper respiratory tract infection			
subjects affected / exposed	11 / 127 (8.66%)	5 / 63 (7.94%)	3 / 63 (4.76%)
occurrences (all)	14	5	3
Sinusitis			
subjects affected / exposed	7 / 127 (5.51%)	2 / 63 (3.17%)	3 / 63 (4.76%)
occurrences (all)	8	2	3
Bronchitis			
subjects affected / exposed	1 / 127 (0.79%)	3 / 63 (4.76%)	2 / 63 (3.17%)
occurrences (all)	1	4	2
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 127 (1.57%)	2 / 63 (3.17%)	3 / 63 (4.76%)
occurrences (all)	2	2	3

Urinary tract infection			
subjects affected / exposed	2 / 127 (1.57%)	1 / 63 (1.59%)	1 / 63 (1.59%)
occurrences (all)	2	1	1
Gastroenteritis viral			
subjects affected / exposed	3 / 127 (2.36%)	2 / 63 (3.17%)	2 / 63 (3.17%)
occurrences (all)	3	2	2
Gastroenteritis			
subjects affected / exposed	2 / 127 (1.57%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	2	2	0
Influenza			
subjects affected / exposed	1 / 127 (0.79%)	2 / 63 (3.17%)	2 / 63 (3.17%)
occurrences (all)	1	2	2
Staphylococcal infection			
subjects affected / exposed	1 / 127 (0.79%)	1 / 63 (1.59%)	2 / 63 (3.17%)
occurrences (all)	1	1	2
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 127 (0.79%)	2 / 63 (3.17%)	0 / 63 (0.00%)
occurrences (all)	1	3	0
Total - Infections and infestations			
subjects affected / exposed	51 / 127 (40.16%)	24 / 63 (38.10%)	28 / 63 (44.44%)
occurrences (all)	77	44	46

Non-serious adverse events	GP2017 continued		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 126 (66.67%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Total - Vascular disorders			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	6 / 126 (4.76%)		
occurrences (all)	8		
Injection site bruising			

subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Injection site pruritus			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Injection site induration			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 126 (2.38%)		
occurrences (all)	3		
Total - General disorders and administration site conditions			
subjects affected / exposed	17 / 126 (13.49%)		
occurrences (all)	27		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	4 / 126 (3.17%)		
occurrences (all)	4		
Total - Immune system disorders			
subjects affected / exposed	4 / 126 (3.17%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	4		
Sinus congestion			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Rhinitis allergic			

subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Total - Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	10 / 126 (7.94%)		
occurrences (all)	15		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Psychiatric disorders			
subjects affected / exposed	7 / 126 (5.56%)		
occurrences (all)	7		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Investigations			
subjects affected / exposed	10 / 126 (7.94%)		
occurrences (all)	11		
Injury, poisoning and procedural complications			
Muscle strain			

subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Injury, poisoning and procedural complications			
subjects affected / exposed	12 / 126 (9.52%)		
occurrences (all)	14		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 126 (10.32%)		
occurrences (all)	20		
Dizziness			
subjects affected / exposed	4 / 126 (3.17%)		
occurrences (all)	4		
Sciatica			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Nervous system disorders			
subjects affected / exposed	23 / 126 (18.25%)		
occurrences (all)	32		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Blood and lymphatic system disorders			
subjects affected / exposed	6 / 126 (4.76%)		
occurrences (all)	7		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Toothache			

subjects affected / exposed	4 / 126 (3.17%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	3 / 126 (2.38%)		
occurrences (all)	4		
Dental caries			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Total - Gastrointestinal disorders			
subjects affected / exposed	11 / 126 (8.73%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	4 / 126 (3.17%)		
occurrences (all)	6		
Pruritus generalised			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Dermal cyst			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		

Dry skin			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Psoriasis			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Total - Skin and subcutaneous tissue disorders			
subjects affected / exposed	15 / 126 (11.90%)		
occurrences (all)	20		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 126 (3.97%)		
occurrences (all)	8		
Back pain			
subjects affected / exposed	5 / 126 (3.97%)		
occurrences (all)	7		
Pain in extremity			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Total - Musculoskeletal and connective tissue disorders			
subjects affected / exposed	20 / 126 (15.87%)		
occurrences (all)	29		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 126 (9.52%)		
occurrences (all)	23		
Upper respiratory tract infection			
subjects affected / exposed	12 / 126 (9.52%)		
occurrences (all)	17		
Sinusitis			
subjects affected / exposed	11 / 126 (8.73%)		
occurrences (all)	13		

Bronchitis			
subjects affected / exposed	7 / 126 (5.56%)		
occurrences (all)	7		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 126 (2.38%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	5 / 126 (3.97%)		
occurrences (all)	6		
Gastroenteritis viral			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Staphylococcal infection			
subjects affected / exposed	0 / 126 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Total - Infections and infestations			
subjects affected / exposed	57 / 126 (45.24%)		
occurrences (all)	107		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2013	Sample size was increased from 360 to 448 patients (based on a 95% CI). An expected difference of 3% was assumed for the sample size calculation. The re-randomization scheme at Week 17 was adjusted to a ratio of 2:1. The eligibility of patients based on their TB status was made more restrictive in exclusion criteria: Patients with a positive QFT at screening were no longer eligible for participation in the study to minimize the risk of possible TB re-activation. Correction of inclusion criterion: all s.c. injections were to be done at the site thus no explanation of self-administration. Assessment of exploratory PD biomarkers was excluded from the study. To standardize the process and to protect patients' privacy, it was clarified that the psoriasis lesions were to be photographed only for specific body parts excluding the face. The instructions of storing GP2017 and Humira separated from other investigational medicinal products were removed as deemed not according to the normal routine. The prohibited regimen of topical corticosteroids was specified based on their levels of potency and instructions on how to determine their level of potency were added. It was added that if a patient prematurely discontinued from Treatment Period 1, the Week 17 visit assessments were to be performed as a discontinuation visit. If a patient prematurely discontinued from Treatment Period 2, the Week 35 visit assessments were to be performedd. An ECG assessment was added to Week 17 to match the assessments at Week 35. Safety laboratory at Screening (to provide a baseline laboratory assessment prior to study drug administration) and at Week 39 and final follow up 6 weeks after last dosing were added. The frequency of urine pregnancy tests performed in women of childbearing potential was increased to a minimum of every 4 weeks. An additional vital signs assessment at Visit 9 (Week 13) together with a physical examination was added.
10 September 2014	The treatment period was extended to follow the current European guidelines (CHMP/EWP/2454/02) and (CHMP/BMWP/42832/2005), requesting one-year follow up data in case of chronic use. Before the amendment, the last drug administration was to take place at Week 33, which was extended by another 8 treatment visits from Week 35 to Week 49, followed by a last study visit at Week 51. During the Extension Period, safety, immunogenicity and efficacy data were to be collected continuously. Patients in the switching arms were to receive the treatment they had been randomized to at the study start throughout the extension period. Some patients had already completed and left the study after Week 35 (as per study protocol after Protocol amendment 2), when Amendment 3 became effective. The treatment-free follow-up period after the last injection of study treatment, to wash-out GP2017 or Humira, was removed and the study was to end after the Extension Period for all patients. Patients were able to receive a standard treatment after the end of the study to avoid potential disease exacerbation. The assay to measure the binding of ADAs used in this study, developed to ensure a high drug tolerance, was considered not necessary. Therefore, the last ADA assessment was to be performed two weeks after last study drug administration at Week 51. To provide additional results on very sensitive endpoints and as complement to the primary PASI75 analysis, the relative change from baseline in the continuous PASI score was to be evaluated until Week 16 and compared using powered MMRM analyses and analyses applying an ATE approach. Patients were allowed to interrupt study treatment administration, if they had an AE that in the opinion of the investigator needed to be sufficiently resolved before study treatment could be administered again. To account for stratification factors in the primary analysis, systemic therapy and body weight categories were to be included in the analysis as covariates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported