Clinical trial results:
A randomized, double-blind, multicenter study to demonstrate equivalent efficacy and to compare safety and immunogenicity of a biosimilar etanercept (GP2015) and Enbrel® in patients with moderate to severe chronic plaque-type psoriasis

Summary

EudraCT number	2012-002011-26
Trial protocol	SK HU CZ GB EE DE BG PL
Global end of trial date	30 March 2015

Results information

Result version number	v1 (current)
This version publication date	31 March 2016
First version publication date	31 March 2016

Trial information

Trial identification

Sponsor protocol code	GP15-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01891864
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sandoz
Sponsor organisation address	Industriestrasse 25, Holzkirchen, Germany, 83607
Public contact	Strategic Planning Biopharma Clinical Development, Sandoz, 0049 8024 / 476 - 0, biopharma.clinicaltrials@sandoz.com
Scientific contact	Strategic Planning Biopharma Clinical Development, Sandoz, 0049 8024 / 476 - 0, 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	19 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2014
Global end of trial reached?	Yes
Global end of trial date	30 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to demonstrate equivalence in efficacy (primarily based on PASI 75 response rate) and similarity in the safety profile of GP2015 and Enbrel® (EU-licensed) in patients with moderate to severe chronic plaque-type psoriasis and to evaluate the effects of repeated switching between GP2015 and Enbrel® on efficacy, overall safety and immunogenicity.

Protection of trial subjects:

This trial was designed, conducted and reported in accordance with the international Conference on Harmonization (!CH) 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, as long as they did not conflict with applicable UK law.
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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 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	Poland: 190
Country: Number of subjects enrolled	Romania: 33
Country: Number of subjects enrolled	Bulgaria: 21
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Estonia: 81
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Ukraine: 42
Country: Number of subjects enrolled	Czech Republic: 41
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Slovakia: 37
Worldwide total number of subjects	531
EEA total number of subjects	467

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)	503
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter, randomized, double-blind, confirmatory safety and efficacy study. In total 774 patients were screened to randomize 531 patients with moderate to severe chronic plaque-type psoriasis. Patients were randomized at 71study centers in 12 countries.

Pre-assignment

Screening details:

Prior to baseline (Treatment Day 1, Visit 2) patients were to undergo an eligibility assessment period of at least 2 weeks and up to a maximum of 4 weeks duration.

Period 1

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

Blinding implementation details:

All treatment assignments were blinded and concealed from patients and investigator site staff. A patient randomization list will be produced by the IRT provider using a validated system. Each patient randomization number is associated with one of the treatment arms.

Arms

Are arms mutually exclusive?	Yes
Arm title	GP2015

Arm description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week12

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	GP2015
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week12
The total number of IMP injections is 24 during Treatment Period 1 (two per week from Treatment Day 1 to Week 12)

Arm title	Enbrel

Arm description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week12

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

Dosage and administration details:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week12
The total number of IMP injections is 24 during Treatment Period 1 (two per week from Treatment Day 1 to Week 12).

Number of subjects in period 1	GP2015	Enbrel
Started	264	267
Completed	256	255
Not completed	8	12
Adverse event, serious fatal	-	1
Consent withdrawn by subject	2	5
Physician decision	-	1
Adverse event, non-fatal	4	4
Lost to follow-up	1	-
Protocol deviation	1	1

Period 2

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

Blinding implementation details:

All treatment assignments were blinded and concealed from patients and investigator site staff. A patient randomization list will be produced by the IRT provider using a validated system. Each patient randomization number is associated with one of the treatment arms.

Arms

Are arms mutually exclusive?	Yes
Arm title	GP2015 continued

Arm description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12

Arm type	Experimental
Investigational medicinal product name	GP2015
Investigational medicinal product code	GP2015
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30.
The total number of IMP injections is 18 during Treatment Period 2 (one per week from Week 13 to Week 30)

Arm title	Enbrel continued

Arm description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12

Arm type	Active comparator

Investigational medicinal product name	Etanercept
Investigational medicinal product code	Enbrel
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30.
The total number of IMP injections is 18 during Treatment Period 2 (one per week from Week 13 to Week 30).

Arm title	GP2015 switched

Arm description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12

Arm type	Experimental
Investigational medicinal product name	GP2015 in period 1/Enbrel/GP 2015/Enbrel
Investigational medicinal product code	GP2015/Enbrel
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

GP2015/Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week 30. Three periods of 6 weeks alternating between Enbrel/GP2015/Enbrel. The total number of IMP injections is 18 during Treatment Period 2 (one per week from Treatment Week 13 to Week 30)

Arm title	Enbrel switched

Arm description:

Enbrel/GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 30

Arm type	Active comparator
Investigational medicinal product name	Enbrel in period 1/GP2015/Enbrel/GP2015
Investigational medicinal product code	Enbrel/GP2015
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Enbrel/GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week 30. Three periods of 6 weeks alternating between GP2015/Enbrel/GP2015. The total number of IMP injections is 18 during Treatment Period 2 (one per week from Treatment Week 13 to Week 30)

Number of subjects in period 2[1]	GP2015 continued	Enbrel continued	GP2015 switched
Started	150	151	100
Completed	143	142	96
Not completed	7	9	4
Consent withdrawn by subject	3	4	1
Physician decision	1	-	-
Adverse event, non-fatal	1	2	-
site termination	1	2	-
termination of site	-	-	2

Lack of efficacy	1	-	1
Protocol deviation	-	1	-

Number of subjects in period 2[1]	Enbrel switched
Started	96
Completed	91
Not completed	5
Consent withdrawn by subject	1
Physician decision	-
Adverse event, non-fatal	4
site termination	-
termination of site	-
Lack of efficacy	-
Protocol deviation	-

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 patients with a PASI50 response at 12 weeks -continuing treatment- were included in treatment period 2.

Period 3

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

Blinding implementation details:

All treatment assignments were blinded and concealed from patients and investigator site staff. A patient randomization list will be produced by the IRT provider using a validated system. Each patient randomization number is associated with one of the treatment arms.

Arms

Are arms mutually exclusive?	Yes
Arm title	GP2015 continued

Arm description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.

Arm type	Experimental
Investigational medicinal product name	GP2015
Investigational medicinal product code	GP2015
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.
The total number of IMP injections is 22 during the Extension Period.

Arm title	Enbrel continued

Arm description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.

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

Dosage and administration details:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.
The total number of IMP injections is 22 during the Extension Period

Arm title	GP2015 switched

Arm description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.

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

Dosage and administration details:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.
The total number of IMP injections is 22 during the Extension Period. They continued the drug last used in treatment period 2.

Arm title	Enbrel switched

Arm description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.

Arm type	Experimental
Investigational medicinal product name	GP2015
Investigational medicinal product code	GP2015
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.
The total number of IMP injections is 22 during the Extension Period. The last drug used in treatment period 2 was continued in the extension period.

Number of subjects in period 3[2]	GP2015 continued	Enbrel continued	GP2015 switched
Started	140	142	95
Completed	132	137	88
Not completed	8	5	7
Consent withdrawn by subject	1	2	4

Adverse event, non-fatal	4	2	2
Pregnancy	1	-	-
Lost to follow-up	2	-	-
Lack of efficacy	-	1	1

Number of subjects in period 3[2]	Enbrel switched
Started	90
Completed	90
Not completed	0
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Pregnancy	-
Lost to follow-up	-
Lack of efficacy	-

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: Only patients completing treatment period 2 and continuing in the extension period participated

Baseline characteristics

Reporting groups	
Reporting group title	GP2015
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week12	
Reporting group title	Enbrel
Reporting group description:	
Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week12	

Reporting group values	GP2015	Enbrel	Total
Number of subjects	264	267	531
Age categorical			
Units: Subjects			
Age 18-64	254	249	503
Age 65-85	10	18	28
Age continuous			
Age treatment period 1			
Units: years			
arithmetic mean	42.1	42.7	
standard deviation	± 12.29	± 12.86	-
Gender categorical			
Male and female numbers			
Units: Subjects			
Female	107	95	202
Male	157	172	329
Weight			
Weight			
Units: kg			
arithmetic mean	86.3	85.9	
standard deviation	± 21.12	± 18.72	-
BMI			
BMI			
Units: kg/m2			
arithmetic mean	28.561	28.0458	
standard deviation	± 6.0953	± 5.4632	-

End points

End points reporting groups

Reporting group title	GP2015
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week12	
Reporting group title	Enbrel
Reporting group description:	
Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week12	
Reporting group title	GP2015 continued
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12	
Reporting group title	Enbrel continued
Reporting group description:	
Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12	
Reporting group title	GP2015 switched
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 12	
Reporting group title	Enbrel switched
Reporting group description:	
Enbrel/GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 13 until Week 30 in patients who had achieved at least a PASI50 response at Week 30	
Reporting group title	GP2015 continued
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.	
Reporting group title	Enbrel continued
Reporting group description:	
Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.	
Reporting group title	GP2015 switched
Reporting group description:	
Enbrel 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.	
Reporting group title	Enbrel switched
Reporting group description:	
GP2015 50 mg subcutaneous (s.c.) injection of study drug from week 31 until Week 52 in patients who had completed treatment period 2.	

Primary: PASI 75 response rate at Week 12 between GP2015 and Enbrel

End point title	PASI 75 response rate at Week 12 between GP2015 and Enbrel
End point description:	
The 95% CI for the PASI 75 response rate differences at Week12 between GP2015 and Enbrel.	
End point type	Primary
End point timeframe:	
The PASI 75 response reate was determined at 12 weeks.	

End point values	GP2015	Enbrel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[1]	241[2]		
Units: percentage				
number (not applicable)	73.4	75.7		

Notes:

[1] - PPS

[2] - PPS

Statistical analyses

Statistical analysis title	95% CI of PASI 75 response difference at week12

Statistical analysis description:

PASI 75 response rate (proportion of patients showing at least a 75% improvement in PASI) after the first 12 weeks of treatment (Treatment Period 1) was the primary endpoint to assess equivalence between GP2015 and Enbrel®. Therapeutic equivalence in terms of PASI75 could be concluded if the exact 95% confidence interval for the difference in the PASI75 rates is completely contained within the interval [−18%; 18%]. A logistic regression model was to be employed.

Comparison groups	GP2015 v Enbrel
Number of subjects included in analysis	480
Analysis specification	Pre-specified
Analysis type	equivalence[3]
P-value	< 0.025
Method	Regression, Logistic
Parameter estimate	95% CI of response rate differences
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.85
upper limit	5.3

Notes:

[3] - The analysis of the primary variable was based on the PPS.

Secondary: % change from baseline in PASI score up to Week12

End point title	% change from baseline in PASI score up to Week12

End point description:

The key sec. efficacy endpoint in TP1 was the % change from baseline in PASI score up to Week12. Two approaches (MMRM and ATE approach) were employed in order to calculate 2-sided 95% CIs for the difference between the treatment groups.

End point type	Secondary

End point timeframe:

Percent change in PASI between baseline to week 12.

End point values	GP2015	Enbrel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	241		
Units: percentage difference				
number (not applicable)	-56.11	-55.48		

Statistical analyses

Statistical analysis title	MMRM method percentage change PASI response 0-12 w

Statistical analysis description:

A MMRM (Mixed Model Repeated Method) was performed on the percentage change from baseline in PASI score from baseline to Week 12. 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 Enbrel was contained within the interval [−15%; 15%].

Comparison groups	GP2015 v Enbrel
Number of subjects included in analysis	480
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.025
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.474
upper limit	2.204

Statistical analysis title	ATE of PASI response from baseline to week 12

Statistical analysis description:

The mean averaged treatment effect (ATE) of percent change from baseline in PASI score up to week 12 was derived for each patient and analyzed using an ANCOVA apporach. 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 Enbrel was contained within the interval [−15%; 15%].

Comparison groups	GP2015 v Enbrel
Number of subjects included in analysis	480
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.025
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.61
upper limit	1.845

Secondary: % Change from baseline in PASI score at the end of treatment period 2

End point title	% Change from baseline in PASI score at the end of treatment period 2

End point description:

Percentage change in PASI score at the end of treatment period 2 at 30 weeks.

End point type	Secondary

End point timeframe:

Between week 0 and week 30

End point values	GP2015 continued	Enbrel continued	GP2015 switched	Enbrel switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137[4]	129[5]	90[6]	88[7]
Units: percentage				
arithmetic mean (standard deviation)	-88.955 (± 12.3509)	-88.885 (± 12.3666)	-88.287 (± 13.5151)	-88.517 (± 13.9095)

Notes:

[4] - PPS

[5] - PPS

[6] - PPS

[7] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: % Change from baseline in PASI score at the end of the extension period

End point title	% Change from baseline in PASI score at the end of the extension period

End point description:

Percentage change in PASI score between baseline and end of the extension period.

End point type	Secondary

End point timeframe:

Between baseline and 52 weeks

End point values	GP2015 continued	Enbrel continued	GP2015 switched	Enbrel switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	126[8]	128[9]	85[10]	87[11]
Units: percentage				
arithmetic mean (standard deviation)	-87.833 (± 16.8661)	-86.597 (± 15.9226)	-85.574 (± 19.4098)	-88.527 (± 15.752)

Notes:
[8] - PPS
[9] - PPS
[10] - PPS
[11] - PPS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PASI 75 response rate at the end of treatment period 2

End point title	PASI 75 response rate at the end of treatment period 2

End point description:
PASI 75 response rate at 30 weeks.

End point type	Other pre-specified

End point timeframe:
At week 30

End point values	GP2015 continued	Enbrel continued	GP2015 switched	Enbrel switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119	112	78	76
Units: percentage				
number (not applicable)	86.9	86.8	86.7	86.4

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PASI 75 response rate at the end of the extension period

End point title	PASI 75 response rate at the end of the extension period

End point description:
PASI 75 response rate at 52 weeks.

End point type	Other pre-specified

End point timeframe:
At week 52

End point values	GP2015 continued	Enbrel continued	GP2015 switched	Enbrel switched
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	104	71	74
Units: percentage				
number (not applicable)	85.7	81.3	83.5	85.1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

To ensure patient safety, every SAE/AE, regardless of suspected causality, occurring after the patient has provided informed consent and until 30 days after the patient has stopped study participation

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	17.0

Reporting groups

Reporting group title	GP2015 continued

Reporting group description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week52

Reporting group title	Enbrel switched

Reporting group description:

GP2015 50 mg subcutaneous (s.c.) injection of study drug until Week52

Reporting group title	GP2015 switched

Reporting group description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week52

Reporting group title	Enbrel continued

Reporting group description:

Enbrel 50 mg subcutaneous (s.c.) injection of study drug until Week52

Serious adverse events	GP2015 continued	Enbrel switched	GP2015 switched
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 164 (6.10%)	6 / 96 (6.25%)	11 / 100 (11.00%)
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)			
Malignant melanoma in situ			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Squamous cell carcinoma of the cervix			

subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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			
Fatigue			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Milk allergy			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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			
Respiratory failure			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
Pulmonary sarcoidosis			

subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Upper limb fracture			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
Lower limb fracture			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
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			
Cardiopulmonary failure	Additional description: Fatal event		
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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
Multiple sclerosis			

subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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			
Umbilical hernia			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric vascular insufficiency			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
Cholelithiasis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
renal failure acute			

subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Pneumonia			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Brain abscess			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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
lobar pneumonia			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	0 / 100 (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 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Diverticulitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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

Tonsillitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	0 / 100 (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
Eczema infected			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (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
Metabolism and nutrition disorders			
Acid-base balance disorder mixed			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Enbrel continued		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 171 (4.09%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the cervix			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Milk allergy			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Meniscus injury			

subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiopulmonary failure	Additional description: Fatal event		
subjects affected / exposed	1 / 171 (0.58%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Umbilical hernia			

subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric vascular insufficiency			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
renal failure acute			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 171 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 171 (0.58%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain abscess				
subjects affected / exposed	1 / 171 (0.58%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
lobar pneumonia				
subjects affected / exposed	1 / 171 (0.58%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 171 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 171 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 171 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eczema infected				
subjects affected / exposed	0 / 171 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acid-base balance disorder mixed				

subjects affected / exposed	0 / 171 (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: 1 %

Non-serious adverse events	GP2015 continued	Enbrel switched	GP2015 switched
Total subjects affected by non-serious adverse events			
subjects affected / exposed	134 / 164 (81.71%)	89 / 96 (92.71%)	99 / 100 (99.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 164 (3.05%)	2 / 96 (2.08%)	3 / 100 (3.00%)
occurrences (all)	5	2	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	2 / 100 (2.00%)
occurrences (all)	0	2	2
Fatigue			
subjects affected / exposed	1 / 164 (0.61%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 164 (1.83%)	0 / 96 (0.00%)	3 / 100 (3.00%)
occurrences (all)	3	0	3
oropharyngeal pain			
subjects affected / exposed	3 / 164 (1.83%)	1 / 96 (1.04%)	3 / 100 (3.00%)
occurrences (all)	3	1	3
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 164 (1.22%)	0 / 96 (0.00%)	4 / 100 (4.00%)
occurrences (all)	2	0	4
Alanine aminotransferase increased			
subjects affected / exposed	6 / 164 (3.66%)	2 / 96 (2.08%)	1 / 100 (1.00%)
occurrences (all)	6	2	1
Aspartate aminotransferase increased			

subjects affected / exposed	5 / 164 (3.05%)	2 / 96 (2.08%)	1 / 100 (1.00%)
occurrences (all)	5	2	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	6 / 164 (3.66%)	0 / 96 (0.00%)	3 / 100 (3.00%)
occurrences (all)	6	0	3
Weight increased			
subjects affected / exposed	2 / 164 (1.22%)	0 / 96 (0.00%)	3 / 100 (3.00%)
occurrences (all)	2	0	3
Blood uric acid increased			
subjects affected / exposed	3 / 164 (1.83%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	3 / 164 (1.83%)	3 / 96 (3.13%)	4 / 100 (4.00%)
occurrences (all)	3	3	4
Somnolence			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Lymphadenopathy			
subjects affected / exposed	4 / 164 (2.44%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	4	1	1
Eye disorders			
Eye haemorrhage			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 164 (2.44%)	3 / 96 (3.13%)	1 / 100 (1.00%)
occurrences (all)	4	3	1

Abdominal pain upper			
subjects affected / exposed	3 / 164 (1.83%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Gastritis			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	2 / 100 (2.00%)
occurrences (all)	0	2	2
Toothache			
subjects affected / exposed	0 / 164 (0.00%)	3 / 96 (3.13%)	0 / 100 (0.00%)
occurrences (all)	0	3	0
Dental caries			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Hepatitis alcoholic			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Pruritus			
subjects affected / exposed	2 / 164 (1.22%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Dermatitis psoriasiform			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Dermatitis allergic			
subjects affected / exposed	3 / 164 (1.83%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	3	0	0
Pruritis generalized			

subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 164 (1.83%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	3	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 164 (3.05%)	5 / 96 (5.21%)	3 / 100 (3.00%)
occurrences (all)	5	5	3
Back pain			
subjects affected / exposed	7 / 164 (4.27%)	4 / 96 (4.17%)	2 / 100 (2.00%)
occurrences (all)	7	4	2
Spinal pain			
subjects affected / exposed	2 / 164 (1.22%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Musculoskeletal pain			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Osteoarthritis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Infections and infestations			
Pharyngitis			
subjects affected / exposed	7 / 164 (4.27%)	3 / 96 (3.13%)	5 / 100 (5.00%)
occurrences (all)	7	3	5
Nasopharyngitis			
subjects affected / exposed	20 / 164 (12.20%)	10 / 96 (10.42%)	14 / 100 (14.00%)
occurrences (all)	20	10	14
Viral upper respiratory tract infection			

subjects affected / exposed	5 / 164 (3.05%)	8 / 96 (8.33%)	4 / 100 (4.00%)
occurrences (all)	5	8	4
Respiratory tract infection viral			
subjects affected / exposed	4 / 164 (2.44%)	1 / 96 (1.04%)	4 / 100 (4.00%)
occurrences (all)	4	1	4
Upper respiratory tract infection			
subjects affected / exposed	4 / 164 (2.44%)	3 / 96 (3.13%)	1 / 100 (1.00%)
occurrences (all)	4	3	1
Rhinitis			
subjects affected / exposed	2 / 164 (1.22%)	3 / 96 (3.13%)	1 / 100 (1.00%)
occurrences (all)	2	3	1
Bronchitis			
subjects affected / exposed	4 / 164 (2.44%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	4	0	0
Tonsillitis			
subjects affected / exposed	5 / 164 (3.05%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	5	1	1
Influenza			
subjects affected / exposed	2 / 164 (1.22%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Oral herpes			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	2 / 164 (1.22%)	1 / 96 (1.04%)	2 / 100 (2.00%)
occurrences (all)	2	1	2
Viral infection			
subjects affected / exposed	3 / 164 (1.83%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	3	1	1
Cystitis			
subjects affected / exposed	3 / 164 (1.83%)	0 / 96 (0.00%)	0 / 100 (0.00%)
occurrences (all)	3	0	0
Conjunctivitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Folliculitis			

subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Herpes simplex			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Pyelonephritis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 96 (1.04%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 164 (0.00%)	2 / 96 (2.08%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Hyperuricaemia			
subjects affected / exposed	0 / 164 (0.00%)	0 / 96 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2

Non-serious adverse events	Enbrel continued		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 171 (69.01%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 171 (4.09%)		
occurrences (all)	7		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
oropharyngeal pain			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	4 / 171 (2.34%)		
occurrences (all)	4		
Blood uric acid increased			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	8 / 171 (4.68%)		
occurrences (all)	8		
Somnolence			

subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye haemorrhage			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	4 / 171 (2.34%)		
occurrences (all)	4		
Toothache			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Hepatitis alcoholic			

subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	5 / 171 (2.92%)		
occurrences (all)	5		
Pruritus			
subjects affected / exposed	4 / 171 (2.34%)		
occurrences (all)	4		
Dermatitis psoriasiform			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences (all)	1		
Pruritis generalized			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 171 (4.09%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		
Spinal pain			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Pharyngitis			
subjects affected / exposed	10 / 171 (5.85%)		
occurrences (all)	10		
Nasopharyngitis			
subjects affected / exposed	17 / 171 (9.94%)		
occurrences (all)	17		
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 171 (3.51%)		
occurrences (all)	6		
Respiratory tract infection viral			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	5 / 171 (2.92%)		
occurrences (all)	5		
Rhinitis			
subjects affected / exposed	4 / 171 (2.34%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		
Tonsillitis			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		

Oral herpes			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	3 / 171 (1.75%)		
occurrences (all)	3		
Viral infection			
subjects affected / exposed	2 / 171 (1.17%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	1 / 171 (0.58%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Herpes simplex			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Pyelonephritis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 171 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			

subjects affected / exposed occurrences (all)	0 / 171 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 September 2013	This protocol is amended to implement advice received from national European Health Authorities, including recommendations to apply a 95% rather than a 90% confidence interval to the primary endpoint and to increase the size of the safety database for continuous treatment with GP2015 in comparison to the reference product. The sample size is increased to 546 randomized patients; the number of study sites is increased accordingly. The re-randomization scheme at week 12 is changed to a ratio of 3:1 instead of 1:1: 75% of patients will continue on their assigned treatment arm (either GP2015 or Enbrel®) whilst 25% will be randomized to receive alternating treatment. The confidence interval is increased to 95%.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported