Clinical trial results:
A Randomized, Double-blind Phase 3 Study to Assess the Efficacy and Safety of ABP 710 Compared to Infliximab in Subjects With Moderate to Severe Rheumatoid Arthritis

Summary

EudraCT number	2014-004704-29
Trial protocol	CZ ES HU DE BG PL
Global end of trial date	13 August 2018

Results information

Result version number	v1 (current)
This version publication date	24 August 2019
First version publication date	24 August 2019

Trial information

Trial identification

Sponsor protocol code	20140111

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02937701
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	13 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the efficacy of ABP 710 compared with US-licensed infliximab.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) regulations and guidelines regarding Good Clinical Practice (GCP), clinical safety data management, and scientific integrity; with United States (US) Food and Drug Administration (FDA) regulations set forth in 21 Code of Federal Regulations Parts 50, 56, and 312; and with European Union (EU) Community Directives 2001/20, 2001/83, 2003/94, and 2005/28 as enacted into local law.
Prior to initiation at each study center, the study protocol was reviewed by an Institutional Review Board (IRB) or Institutional Ethics Committee (IEC).
All subjects were to provide written informed consent prior to entering the study and before initiation of any study-related procedure (including administration of investigational product). The investigator was responsible for explaining the benefits and risks of participation in the study to each subject or the subject's legally acceptable representative and for obtaining written informed consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2016
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: 258
Country: Number of subjects enrolled	Czech Republic: 101
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Bulgaria: 25
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United States: 104
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Australia: 9
Worldwide total number of subjects	558
EEA total number of subjects	442

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)	434
From 65 to 84 years	124
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 75 centers in Australia, Bulgaria, Canada, Czech Republic, Germany, Hungary, Poland, Spain, and the United States.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive ABP 710 or infliximab, stratified by geographic region and prior biologic use.
At week 22 participants initially randomized to infliximab were re-randomized in a 1:1 ratio to continue infliximab or switch to ABP 710. Participants initially randomized to ABP 710 continued receiving ABP 710.

Period 1

Period 1 title	Day 1 to Week 22
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	ABP 710

Arm description:

Participants randomized to receive a 3 mg/kg intravenous (IV) infusion of ABP 710 on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.

Arm type	Experimental
Investigational medicinal product name	ABP 710
Investigational medicinal product code	ABP 710
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3-mg/kg IV infusion on day 1 (week 0), at weeks 2 and 6, and every 8 weeks thereafter.

Arm title	Infliximab

Arm description:

Participants randomized to receive 3 mg/kg IV infusion of infliximab on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.

Arm type	Active comparator
Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	Remicade®
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3-mg/kg IV infusion on day 1 (week 0), at weeks 2 and 6, and every 8 weeks thereafter.

Number of subjects in period 1	ABP 710	Infliximab
Started	279	279
Received Treatment	278	278
Completed	244	240
Not completed	35	39
Adverse event, serious fatal	1	1
Consent withdrawn by subject	6	6
Physician decision	2	-
Dissatisfied with Treatment Efficacy	5	9
Adverse event, non-fatal	11	14
Other	1	-
Protocol Specified Criteria	7	7
Lost to follow-up	1	1
Protocol deviation	1	1

Period 2	
Period 2 title	Week 22 to Week 50
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	ABP 710 / ABP 710

Arm description:

At week 22 participants initially randomized to ABP 710 continued receiving 3 mg/kg ABP 710 every 8 weeks through week 46.

Arm type	Experimental
Investigational medicinal product name	ABP 710
Investigational medicinal product code	ABP 710
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3-mg/kg IV infusion administered every 8 weeks

Arm title	Infliximab / Infliximab

Arm description:

At week 22 participants initially randomized to infliximab were re-randomized to continue receiving 3 mg/kg infliximab every 8 weeks through week 46.

Arm type	Active comparator

Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	Remicade®
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3-mg/kg IV infusion administered every 8 weeks

Arm title	Infliximab / ABP 710

Arm description:

At week 22 participants initially randomized to infliximab were re-randomized to receive 3 mg/kg ABP 710 every 8 weeks through week 46.

Arm type	Experimental
Investigational medicinal product name	ABP 710
Investigational medicinal product code	ABP 710
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3-mg/kg IV infusion administered every 8 weeks

Number of subjects in period 2	ABP 710 / ABP 710	Infliximab / Infliximab	Infliximab / ABP 710
Started	244	121	119
Completed	212	113	110
Not completed	32	8	9
Consent withdrawn by subject	8	2	1
Physician decision	2	-	1
Dissatisfied with Treatment Efficacy	10	3	2
Adverse event, non-fatal	10	3	3
Other	-	-	1
Lost to follow-up	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ABP 710
Reporting group description:	
Participants randomized to receive a 3 mg/kg intravenous (IV) infusion of ABP 710 on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	
Reporting group title	Infliximab
Reporting group description:	
Participants randomized to receive 3 mg/kg IV infusion of infliximab on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	

Reporting group values	ABP 710	Infliximab	Total
Number of subjects	279	279	558
Age, Customized Units: Subjects			
< 65 years	217	217	434
≥ 65 years	62	62	124
Age Continuous Units: years			
arithmetic mean	55.0	54.8	
standard deviation	± 11.72	± 11.42	-
Sex: Female, Male Units: Subjects			
Female	214	223	437
Male	65	56	121
Race/Ethnicity, Customized Units: Subjects			
White	265	267	532
Black or African American	12	12	24
Asian	2	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	18	13	31
Not Hispanic or Latino	261	266	527
Unknown or Not Reported	0	0	0
Geographic Region Units: Subjects			
Asia Pacific	5	4	9
Europe	220	222	442
North America	54	53	107
Prior Biologic Use for Rheumatoid Arthritis Units: Subjects			
Yes	77	81	158
No	202	198	400
Duration of Rheumatoid Arthritis (RA) Units: years			
arithmetic mean	8.72	8.34	
standard deviation	± 7.914	± 7.604	-

Swollen joint Count			
A total of 66 joints were scored for presence or absence of swelling.			
Units: joints			
arithmetic mean	14.595	14.730	
standard deviation	± 8.0507	± 8.8315	-
Tender Joint Count			
A total of 68 joints were scored for presence or absence of tenderness.			
Units: joints			
arithmetic mean	23.109	23.764	
standard deviation	± 12.1648	± 13.3800	-
Patient Global Health Assessment			
The participant's overall assessment of their disease activity in the past week assessed on a 100 mm visual analog scale (VAS), where 0 mm = No RA activity at all and 100 mm = Worst RA activity imaginable.			
Units: mm			
arithmetic mean	65.4	64.1	
standard deviation	± 18.13	± 20.03	-
Investigator's Global Health Assessment			
The investigator's assessment of the participant's current disease activity assessed on a 100 mm VAS where 0 mm = no activity at all (symptom-free and no arthritis symptoms) and 100 mm = worst activity imaginable (maximum arthritis disease activity).			
Units: mm			
arithmetic mean	64.5	64.1	
standard deviation	± 15.88	± 15.76	-
Patient's Assessment of Disease-related Pain			
The participant's assessment of their current level of pain assessed on a 100 mm horizontal VAS, where 0 mm = no pain at all and 100 mm = worst pain imaginable.			
Units: mm			
arithmetic mean	63.5	61.5	
standard deviation	± 20.30	± 21.65	-
Disability Index of the Health Assessment Questionnaire (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire consisting of 20 questions in eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability.			
Units: units on a scale			
arithmetic mean	1.44	1.42	
standard deviation	± 0.584	± 0.617	-
C-reactive Protein (CRP) Concentration			
C-reactive protein (CRP) is a protein found in blood. CRP levels rise in response to inflammation.			
Units: mg/L			
arithmetic mean	14.26	14.64	
standard deviation	± 20.171	± 23.117	-

End points

End points reporting groups

Reporting group title	ABP 710
Reporting group description:	
Participants randomized to receive a 3 mg/kg intravenous (IV) infusion of ABP 710 on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	
Reporting group title	Infliximab
Reporting group description:	
Participants randomized to receive 3 mg/kg IV infusion of infliximab on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	
Reporting group title	ABP 710 / ABP 710
Reporting group description:	
At week 22 participants initially randomized to ABP 710 continued receiving 3 mg/kg ABP 710 every 8 weeks through week 46.	
Reporting group title	Infliximab / Infliximab
Reporting group description:	
At week 22 participants initially randomized to infliximab were re-randomized to continue receiving 3 mg/kg infliximab every 8 weeks through week 46.	
Reporting group title	Infliximab / ABP 710
Reporting group description:	
At week 22 participants initially randomized to infliximab were re-randomized to receive 3 mg/kg ABP 710 every 8 weeks through week 46.	

Primary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 22

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 22
End point description:	
The primary efficacy endpoint was the response difference (RD) of 20% improvement in ACR core set measurements (ACR20) at week 22. A positive ACR20 response is defined if the following 3 criteria for improvement from baseline were met: • ≥ 20% improvement in 68 tender joint count; • ≥ 20% improvement in 66 swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global health assessment (measured on a 100 mm VAS); ◦ Investigator's global health assessment (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]); ◦ C-reactive protein concentration. The analysis was conducted in the intent-to-treat population which consisted of all randomized participants. Participants with missing data were counted as non-responders (non-responder imputation).	
End point type	Primary
End point timeframe:	
Baseline and week 22	

End point values	ABP 710	Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	279		
Units: percentage of participants				
number (confidence interval 95%)	68.1 (62.63 to 73.57)	59.1 (53.37 to 64.91)		

Statistical analyses

Statistical analysis title	Primary Analysis of ACR20 at Week 22

Statistical analysis description:

For the primary analysis of ACR20, the response difference (RD) was estimated by the Mantel-Haenszel (MH) estimate and the 90% confidence intervals (CIs) of RD were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use for RA).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Response Difference
Point estimate	9.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.67
upper limit	15.96

Notes:

[1] - Clinical equivalence for the primary endpoint was to be evaluated sequentially by first comparing the 2-sided 90% CI for RD of ACR20 at week 22 between ABP 710 and infliximab with an equivalence margin of (-15%, 15%). If the first test was successful, RD of ACR20 at week 22 was to be further evaluated by comparing the 2-sided 90% CI between ABP 710 and infliximab with an equivalence margin of (-12%, 15%).

Statistical analysis title	Sensitivity Analysis of ACR20 at Week 22

Statistical analysis description:

A sensitivity analysis with the RD estimate and CIs for RD of ACR20 estimated using a generalized linear model with geographic region and prior biologic use for RA as covariates was also conducted.

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	Response Difference
Point estimate	9.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.67
upper limit	15.92

Notes:

[2] - Clinical equivalence for the primary endpoint was to be evaluated sequentially by first comparing the 2-sided 90% CI for RD of ACR20 at week 22 between ABP 710 and infliximab with an equivalence margin of (-15%, 15%). If the first test was successful, RD of ACR20 at week 22 was to be further evaluated by comparing the 2-sided 90% CI between ABP 710 and infliximab with an equivalence

margin of (-12%, 15%).

Statistical analysis title	Post-hoc Analysis of ACR20 at Week 22

Statistical analysis description:

A post-hoc analysis was conducted to adjust for the impact of random imbalance in baseline demographic and disease characteristics between the 2 treatment groups. The MH estimate of RD and corresponding CIs were estimated using a nonparametric analysis of covariance method with stratification factors geographic region and prior biologic use, and adjustment for baseline covariates (ACR core set, age, use of oral corticosteroid, use of NSAID, body mass index categories, and methotrexate dose).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	Response Difference
Point estimate	7.184
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.748
upper limit	13.62

Notes:

[3] - Clinical equivalence for the primary endpoint was to be evaluated sequentially by first comparing the 2-sided 90% CI for RD of ACR20 at week 22 between ABP 710 and infliximab with an equivalence margin of (-15%, 15%). If the first test was successful, RD of ACR20 at week 22 was to be further evaluated by comparing the 2-sided 90% CI between ABP 710 and infliximab with an equivalence margin of (-12%, 15%).

Secondary: Percentage of Participants With an ACR20 Response Through Week 14

End point title	Percentage of Participants With an ACR20 Response Through Week 14

End point description:

A positive ACR20 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 20% improvement in 68 tender joint count;
- ≥ 20% improvement in 66 swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global health assessment (measured on a 100 mm VAS);
  - Investigator's global health assessment (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

The analysis was conducted using the intent-to-treat population; participants with missing data at a given time point were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 6, and 14

End point values	ABP 710	Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	279		
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	46.2 (40.39 to 52.09)	38.0 (32.30 to 43.69)		
Week 6	64.9 (59.27 to 70.48)	59.9 (54.10 to 65.61)		
Week 14	66.3 (60.76 to 71.85)	60.2 (54.47 to 65.96)		

Statistical analyses

Statistical analysis title	Response Difference at Week 2

Statistical analysis description:

The response difference at week 2 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	8.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.15
upper limit	14.81

Statistical analysis title	Response Difference at Week 14

Statistical analysis description:

The response difference at week 14 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Response Difference
Point estimate	9.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.51
upper limit	12.87

Statistical analysis title	Response Difference at Week 6

Statistical analysis description:

The response difference at week 6 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	4.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.8
upper limit	11.64

Secondary: Percentage of Participants With an ACR20 Response After Week 22

End point title	Percentage of Participants With an ACR20 Response After Week 22

End point description:

A positive ACR20 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 20% improvement in 68 tender joint count;
- ≥ 20% improvement in 66 swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global health assessment (measured on a 100 mm VAS);
  - Investigator's global health assessment (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

The analysis was conducted in participants re-randomized at week 22 (includes participants initially randomized to ABP 710 who continued treatment with ABP 710 at week 22); participants with missing data at a given visit were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 30, 34, 38, 46, and 50

End point values	ABP 710 / ABP 710	Infliximab / Infliximab	Infliximab / ABP 710	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	244	121	119	
Units: percentage of participants				
number (confidence interval 95%)				
Week 30	69.7 (63.90 to 75.44)	66.9 (58.56 to 75.32)	74.8 (66.99 to 82.59)	
Week 34	74.6 (69.13 to 80.05)	71.1 (63.00 to 79.15)	74.8 (66.99 to 82.59)	

Week 38	70.5 (64.77 to 76.21)	69.4 (61.21 to 77.63)	72.3 (64.23 to 80.31)	
Week 46	61.9 (55.79 to 67.98)	65.3 (56.81 to 73.77)	66.4 (57.90 to 74.87)	
Week 50	67.6 (61.75 to 73.49)	72.7 (64.79 to 80.66)	70.6 (62.40 to 78.77)	

Statistical analyses

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	3.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.26
upper limit	11.73

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	8.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.18
upper limit	17.97

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by

the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	3.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.61
upper limit	11.7

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	4.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.4
upper limit	13.4

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	0.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.34
upper limit	9.4

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	2.79
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.86
upper limit	12.34

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-3.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.27
upper limit	5.17

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710

Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	1.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.89
upper limit	11.08

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Response Difference
Point estimate	-5.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.24
upper limit	3.29

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-1.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.01
upper limit	8.04

Secondary: Percentage of Participants With an ACR50 Response Through Week 22

End point title	Percentage of Participants With an ACR50 Response Through Week 22

End point description:

A positive ACR50 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 50% improvement in 68 tender joint count;
- ≥ 50% improvement in 66 swollen joint count; and
- ≥ 50% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global health assessment (measured on a 100 mm VAS);
  - Investigator's global health assessment (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

The analysis was conducted in the intent-to-treat population; participants with missing data at a given time point were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 6, 14, and 22

End point values	ABP 710	Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	279		
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	17.2 (12.78 to 21.63)	12.5 (8.66 to 16.43)		
Week 6	30.1 (24.72 to 35.49)	28.3 (23.03 to 33.60)		
Week 14	39.4 (33.69 to 45.16)	36.9 (31.25 to 42.58)		
Week 22	43.0 (37.20 to 48.82)	36.2 (30.56 to 41.84)		

Statistical analyses

Statistical analysis title	Response Difference at Week 2

Statistical analysis description:

The response difference at week 2 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	4.41

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.56
upper limit	9.38

Statistical analysis title	Response Difference at Week 6

Statistical analysis description:

The response difference at week 6 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	1.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.71
upper limit	7.94

Statistical analysis title	Response Difference at Week 14

Statistical analysis description:

The response difference at week 14 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.45
upper limit	9.03

Statistical analysis title	Response Difference at Week 22

Statistical analysis description:

The response difference at week 22 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	7.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.27
upper limit	13.83

Secondary: Percentage of Participants With an ACR50 Response After Week 22

End point title	Percentage of Participants With an ACR50 Response After Week 22

End point description:

A positive ACR50 response is defined if the following 3 criteria for improvement from baseline were met:
• ≥ 50% improvement in 68 tender joint count;
• ≥ 50% improvement in 66 swollen joint count; and
• ≥ 50% improvement in at least 3 of the 5 following parameters:
◦ Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
◦ Patient's global health assessment (measured on a 100 mm VAS);
◦ Investigator's global health assessment (measured on a 100 mm VAS);
◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
◦ C-reactive protein concentration.
The analysis was conducted in participants re-randomized at week 22 (includes participants initially randomized to ABP 710 who continued treatment with ABP 710 at week 22); participants with missing data at a given visit were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 30, 34, 38, 46, and 50

End point values	ABP 710 / ABP 710	Infliximab / Infliximab	Infliximab / ABP 710	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	244	121	119	
Units: percentage of participants				
number (confidence interval 95%)				
Week 30	43.0 (36.82 to 49.25)	44.6 (35.77 to 53.49)	47.1 (38.09 to 56.03)	
Week 34	52.5 (46.19 to 58.73)	46.3 (37.40 to 55.17)	56.3 (47.39 to 65.21)	
Week 38	48.0 (41.68 to 54.22)	47.1 (38.21 to 56.00)	49.6 (40.60 to 58.56)	
Week 46	43.9 (37.63 to 50.08)	44.6 (35.77 to 53.49)	50.4 (41.44 to 59.40)	
Week 50	49.2 (42.91 to 55.45)	54.5 (45.67 to 63.42)	57.1 (48.25 to 66.03)	

Statistical analyses

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-1.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.4
upper limit	7.62

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	3.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.28
upper limit	13.67

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab

Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	6.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.62
upper limit	15.48

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	10.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.12
upper limit	21.03

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	0.56
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.54
upper limit	9.59

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	2.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.62
upper limit	13.39

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.11
upper limit	7.93

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	6.14

Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.44
upper limit	16.54

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-5.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.39
upper limit	3.71

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	2.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.51
upper limit	13.37

Secondary: Percentage of Participants With an ACR70 Response Through Week 22

End point title	Percentage of Participants With an ACR70 Response Through Week 22

End point description:

A positive ACR70 response is defined if the following 3 criteria for improvement from baseline were met:

- ≥ 70% improvement in 68 tender joint count;
- ≥ 70% improvement in 66 swollen joint count; and
- ≥ 70% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global health assessment (measured on a 100 mm VAS);
  - Investigator's global health assessment (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

The analysis was conducted in the intent-to-treat population; participants with missing data at a given visit were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 6, 14, and 22

End point values	ABP 710	Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	279		
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	3.9 (1.66 to 6.23)	6.5 (3.57 to 9.33)		
Week 6	14.3 (10.22 to 18.45)	16.5 (12.13 to 20.84)		
Week 14	21.9 (17.01 to 26.71)	16.1 (11.81 to 20.44)		
Week 22	24.0 (19.00 to 29.03)	19.7 (15.05 to 24.38)		

Statistical analyses

Statistical analysis title	Response Difference at Week 2

Statistical analysis description:

The response difference at week 2 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-2.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.84
upper limit	0.83

Statistical analysis title	Response Difference at Week 6
Statistical analysis description:	
The response difference at week 6 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).	
Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-2.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.47
upper limit	2.64

Statistical analysis title	Response Difference at Week 14
Statistical analysis description:	
The response difference at week 14 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).	
Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	5.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	10.91

Statistical analysis title	Response Difference at Week 22
Statistical analysis description:	
The response difference at week 22 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).	
Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	4.58

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.21
upper limit	10.34

Secondary: Percentage of Participants With an ACR70 Response After Week 22

End point title	Percentage of Participants With an ACR70 Response After Week 22

End point description:

A positive ACR70 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 70% improvement in 68 tender joint count;
- ≥ 70% improvement in 66 swollen joint count; and
- ≥ 70% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of disease-related pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global health assessment (measured on a 100 mm VAS);
  - Investigator's global health assessment (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

The analysis was conducted in participants re-randomized at week 22 (includes participants initially randomized to ABP 710 who continued treatment with ABP 710 at week 22); participants with missing data at a given visit were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 30, 34, 38, 46, and 50

End point values	ABP 710 / ABP 710	Infliximab / Infliximab	Infliximab / ABP 710	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	244	121	119	
Units: percentage of participants				
number (confidence interval 95%)				
Week 30	26.6 (21.09 to 32.19)	26.4 (18.59 to 34.30)	26.1 (18.16 to 33.94)	
Week 34	29.5 (23.79 to 35.23)	28.1 (20.09 to 36.11)	35.3 (26.71 to 43.88)	
Week 38	29.1 (23.40 to 34.80)	29.8 (21.61 to 37.90)	32.8 (24.34 to 41.21)	
Week 46	29.5 (23.79 to 35.23)	29.8 (21.61 to 37.90)	37.0 (28.30 to 45.65)	
Week 50	34.0 (28.07 to 39.96)	32.2 (23.90 to 40.56)	43.7 (34.79 to 52.61)	

Statistical analyses

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe

confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.12
upper limit	8.02

Statistical analysis title	Response Difference at Week 30

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 30 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.39
upper limit	9.28

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	1.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7
upper limit	9.51

Statistical analysis title	Response Difference at Week 34

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 34 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	7.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.39
upper limit	17.22

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.03
upper limit	7.59

Statistical analysis title	Response Difference at Week 38

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 38 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710

Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	3.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.41
upper limit	13.14

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	-0.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.98
upper limit	7.66

Statistical analysis title	Response Difference at Week 46

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 46 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	7.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.13
upper limit	17.68

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (ABP 710/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	1.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.81
upper limit	10.29

Statistical analysis title	Response Difference at Week 50

Statistical analysis description:

The response difference (Infliximab/ABP 710 minus Infliximab/Infliximab) at week 50 was estimated by the Mantel-Haenszel estimate; 90% confidence intervals were estimated from the stratified Newcombe confidence limits, adjusting for actual stratification factors (geographic region and prior biologic use).

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Response Difference
Point estimate	12.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.74
upper limit	22.04

Secondary: Change from Baseline in Disease Activity Score 28 (DAS28) Through Week 22

End point title	Change from Baseline in Disease Activity Score 28 (DAS28) Through Week 22

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables:
• 28 tender joint count
• 28 swollen joint count
• C-reactive protein (CRP)
• Patient's global health assessment measured on a 100 mm VAS, where 0 mm = no RA activity and 100 mm = worst RA activity imaginable.
DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission.
The analysis was conducted in the intent-to-treat population with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 6, 14, and 22

End point values	ABP 710	Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	279		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (N = 260, 255)	-1.36 (± 0.991)	-1.29 (± 1.006)		
Week 6 (N = 259,253)	-1.82 (± 1.222)	-1.82 (± 1.203)		
Week 14 (N = 253, 250)	-1.95 (± 1.218)	-1.91 (± 1.289)		
Week 22 (N = 245, 243)	-2.06 (± 1.290)	-2.06 (± 1.296)		

Statistical analyses

Statistical analysis title	Mean Difference at Week 2

Statistical analysis description:

Week 2 difference between means (ABP 710 minus infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.2
upper limit	0.007

Statistical analysis title	Mean Difference at Week 6

Statistical analysis description:

Week 6 difference between means (ABP 710 minus infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 v Infliximab

Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.17
upper limit	0.16

Statistical analysis title	Mean Difference at Week 14

Statistical analysis description:

Week 14 difference between means (ABP 710 minus infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.21
upper limit	0.14

Statistical analysis title	Mean Difference at Week 22

Statistical analysis description:

Week 22 difference between means (ABP 710 minus infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 v Infliximab
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.2
upper limit	0.17

Secondary: Change from Baseline in Disease Activity Score 28 (DAS28) After Week 22

End point title	Change from Baseline in Disease Activity Score 28 (DAS28) After Week 22

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables:
• 28 tender joint count
• 28 swollen joint count
• C-reactive protein (CRP)
• Patient's global health assessment measured on a 100 mm VAS, where 0 mm = no RA activity and 100 mm = worst RA activity imaginable.
DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission.
The analysis was conducted in participants re-randomized at week 22 (includes participants initially randomized to ABP 710 who continued treatment with ABP 710 at week 22) with available data.

End point type	Secondary

End point timeframe:

Baseline and weeks 30, 34, 38, 46, and 50

End point values	ABP 710 / ABP 710	Infliximab / Infliximab	Infliximab / ABP 710	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	244	121	119	
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 30 (N = 225, 112, 112)	-2.07 (± 1.278)	-2.25 (± 1.379)	-2.22 (± 1.266)	
Week 34 (N = 222, 113, 111)	-2.32 (± 1.306)	-2.46 (± 1.372)	-2.45 (± 1.309)	
Week 38 (N = 219, 114, 110)	-2.20 (± 1.277)	-2.27 (± 1.301)	-2.32 (± 1.400)	
Week 46 (N = 205, 108, 108)	-2.11 (± 1.381)	-2.27 (± 1.387)	-2.26 (± 1.440)	
Week 50 (N = 203, 110, 107)	-2.45 (± 1.365)	-2.49 (± 1.276)	-2.64 (± 1.328)	

Statistical analyses

Statistical analysis title	Mean Difference at Week 30

Statistical analysis description:

Week 30 difference between means (ABP 710/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab

Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.08
upper limit	0.4

Statistical analysis title	Mean Difference at Week 30

Statistical analysis description:

Week 30 difference between means (Infliximab/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.27
upper limit	0.28

Statistical analysis title	Mean Difference at Week 34

Statistical analysis description:

Week 34 difference between means (ABP 710/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.12
upper limit	0.35

Statistical analysis title	Mean Difference at Week 34

Statistical analysis description:

Week 34 difference between means (Infliximab/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.3
upper limit	0.24

Statistical analysis title	Mean Difference at Week 38

Statistical analysis description:

Week 38 difference between means (ABP 710/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.18
upper limit	0.3

Statistical analysis title	Mean Difference at Week 38

Statistical analysis description:

Week 38 difference between means (Infliximab/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710

Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.36
upper limit	0.2

Statistical analysis title	Mean Difference at Week 46

Statistical analysis description:

Week 46 difference between means (ABP 710/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.14
upper limit	0.37

Statistical analysis title	Mean Difference at Week 46

Statistical analysis description:

Week 46 difference between means (Infliximab/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	0.25

Statistical analysis title	Mean Difference at Week 50

Statistical analysis description:

Week 50 difference between means (ABP 710/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	ABP 710 / ABP 710 v Infliximab / Infliximab
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.24
upper limit	0.24

Statistical analysis title	Mean Difference at Week 50

Statistical analysis description:

Week 50 difference between means (Infliximab/ABP 710 minus Infliximab/Infliximab) and 90% CIs for difference between means were based on ANCOVA model with the DAS28-CRP change from baseline as the response and adjusted for the baseline DAS28-CRP measurement and the actual stratification factors: geographic region and prior biologic use for RA.

Comparison groups	Infliximab / Infliximab v Infliximab / ABP 710
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference
Point estimate	-0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.47
upper limit	0.08

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to week 22 (initial ABP 710 and infliximab treatment groups) and from week 22 to week 50 for participants re-randomized at week 22, or up to 28 days after last dose for participants who discontinued early.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	ABP 710
Reporting group description:	
Participants received 3 mg/kg intravenous (IV) infusion of ABP 710 on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	
Reporting group title	Infliximab
Reporting group description:	
Participants received 3 mg/kg IV infusion of infliximab on day 1, at weeks 2 and 6, and every 8 weeks thereafter until week 22.	
Reporting group title	ABP 710 / ABP 710
Reporting group description:	
At week 22 participants initially randomized to ABP 710 continued receiving 3 mg/kg ABP 710 every 8 weeks through week 46.	
Reporting group title	Infliximab / Infliximab
Reporting group description:	
At week 22 participants initially randomized to infliximab were re-randomized to continue receiving 3 mg/kg infliximab every 8 weeks through week 46.	
Reporting group title	Infliximab / ABP 710
Reporting group description:	
At week 22 participants initially randomized to infliximab were re-randomized to receive 3 mg/kg ABP 710 every 8 weeks through week 46.	

Serious adverse events	ABP 710	Infliximab	ABP 710 / ABP 710
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 278 (3.24%)	14 / 278 (5.04%)	15 / 241 (6.22%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Endometrial adenocarcinoma			

subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Malignant melanoma			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian low malignant potential tumour			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 278 (0.00%)	2 / 278 (0.72%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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

Non-cardiac chest pain			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Myocardial infarction			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Ventricular extrasystoles			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Blood and lymphatic system disorders			

Iron deficiency anaemia			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Microcytic anaemia			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Constipation			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Pancreatitis acute			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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			
Jaundice cholestatic			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Renal failure			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Ureterolithiasis			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Foot deformity			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	0 / 241 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthritis bacterial			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Cellulitis			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (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
Gastroenteritis			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Pneumonia legionella			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Pneumonia pneumococcal			
subjects affected / exposed	1 / 278 (0.36%)	0 / 278 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 278 (0.00%)	1 / 278 (0.36%)	0 / 241 (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
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 278 (0.00%)	0 / 278 (0.00%)	1 / 241 (0.41%)
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	Infliximab / Infliximab	Infliximab / ABP 710	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 121 (3.31%)	1 / 119 (0.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian low malignant potential tumour			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic hypotension			

subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 121 (0.83%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			

subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 119 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis acute			
subjects affected / exposed	1 / 121 (0.83%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	1 / 121 (0.83%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 121 (0.83%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			

subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 119 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 121 (0.00%)	0 / 119 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ABP 710	Infliximab	ABP 710 / ABP 710
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 278 (17.27%)	32 / 278 (11.51%)	52 / 241 (21.58%)
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	14 / 278 (5.04%)	11 / 278 (3.96%)	23 / 241 (9.54%)
occurrences (all)	14	11	23
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 278 (4.32%)	4 / 278 (1.44%)	13 / 241 (5.39%)
occurrences (all)	12	4	13
Pharyngitis			

subjects affected / exposed	8 / 278 (2.88%)	3 / 278 (1.08%)	2 / 241 (0.83%)
occurrences (all)	8	3	2
Upper respiratory tract infection			
subjects affected / exposed	17 / 278 (6.12%)	18 / 278 (6.47%)	23 / 241 (9.54%)
occurrences (all)	18	18	26

Non-serious adverse events	Infliximab / Infliximab	Infliximab / ABP 710	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 121 (23.14%)	30 / 119 (25.21%)	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	9 / 121 (7.44%)	7 / 119 (5.88%)	
occurrences (all)	10	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 121 (9.09%)	8 / 119 (6.72%)	
occurrences (all)	12	10	
Pharyngitis			
subjects affected / exposed	2 / 121 (1.65%)	7 / 119 (5.88%)	
occurrences (all)	2	7	
Upper respiratory tract infection			
subjects affected / exposed	9 / 121 (7.44%)	14 / 119 (11.76%)	
occurrences (all)	9	16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2017	- Clarified the premedication requirement. - Specified that subjects who were unable to complete the week 22 visit within the allowed window were to be discontinued from the study and that these subjects should return for an EOS visit to complete the EOS assessments within 28 days, if possible. - Specified that subjects who were unable to complete the screening procedures within 28 days before baseline would be considered screen failures. Specified that these subjects could be rescreened, and they may be rescreened under the same informed consent form if rescreening occurred within 30 days. - Removed "adverse events" from the list of examples of "Reasons for removal of a subject from the study." - Emphasized that preinfusion PK samples were required to be drawn within 1 hour before dosing and that end-of-infusion PK samples were required to be collected within 10 minutes of completing the infusion. - Specified that 95% CIs, in addition to 90% CIs, would be presented for efficacy endpoints. - Clarified the inclusion and exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported