Clinical trial results:
A Randomized, Double-blind, Phase 3 Study of ABP 501 Efficacy and Safety Compared to Adalimumab in Subjects with Moderate to Severe Rheumatoid Arthritis

Summary

EudraCT number	2013-000525-31
Trial protocol	GB CZ ES DE HU PL BG RO
Global end of trial date	19 November 2014

Results information

Result version number	v1 (current)
This version publication date	25 June 2016
First version publication date	25 June 2016

Trial information

Trial identification

Sponsor protocol code	20120262

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01970475
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	19 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study is to assess the efficacy of ABP 501 compared with adalimumab.

Protection of trial subjects:

This study was conducted in accordance with the Note for Guidance on GCP (ICH Harmonised Tripartite Guideline E6 [R1]; FDA CFR [21 CFR § 50, 56, 312]), the general guidelines indicated in the Declaration of Helsinki and all applicable regulatory requirements.
This study was conducted in compliance with Institutional Review Board (IRB)/Independent Ethics Committee (IEC) and ICH GCP Guidelines - including Title 21 Part 56 of the US Code of Federal Regulations (CFR) relating to IRBs/IECs and GCP as described in the US FDA Code of Federal Regulations CFR (21 CFR § 50, 56, 312) - in accordance with applicable ICH regulations regarding clinical safety data management (E2A, E2B[R3]), European Community directives 2001/20, 2001/83, 2003/94 and 2005/28 as enacted into local law, and with ICH guidelines regarding scientific integrity (E4, E8, E9, and E10). In addition, this study was conducted in adherence to all local regulatory requirements, and requirements for data protection.
Before initiating the study, the investigator/institution obtained written and dated approval/favorable opinion from the IRB/IEC for the study protocol/amendments, written informed consent form, any consent form updates, subject recruitment procedures (eg, advertisements), and any written information provided to subjects and a statement from the IRB/IEC that they comply with GCP requirements.
The investigator explained the benefits and risks of participation in the study to each subject or the subject’s legally acceptable representative and obtained written informed consent before the subject entered the study and before initiation of any study related procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 197
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Bulgaria: 19
Country: Number of subjects enrolled	Czech Republic: 58
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Hungary: 57
Country: Number of subjects enrolled	Russian Federation: 2

Country: Number of subjects enrolled	United States: 137
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Mexico: 3
Worldwide total number of subjects	526
EEA total number of subjects	377

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)	402
From 65 to 84 years	124
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a randomized, double-blind, active comparator-controlled study of adalimumab-naïve adults with moderate to severe rheumatoid arthritis (RA) who had an inadequate response to methotrexate (MTX).
This study was conducted at 92 centers in 12 countries.

Pre-assignment

Screening details:

Participants were randomized 1:1 to receive either ABP 501 or adalimumab at 40 mg every 2 weeks for 22 weeks. The assessment of the primary endpoint was at week 24, with a safety follow-up period through week 26. Randomization was stratified by geographic region and prior biologic use for RA (capped at 40% of the study population).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	ABP 501

Arm description:

Participants received ABP 501 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.

Arm type	Experimental
Investigational medicinal product name	ABP 501
Investigational medicinal product code	ABP 501
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg subcutaneous injection every 2 weeks

Arm title	Adalimumab

Arm description:

Participants received adalimumab 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.

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

Dosage and administration details:

40 mg subcutaneous injection every 2 weeks

Number of subjects in period 1	ABP 501	Adalimumab
Started	264	262
Completed	243	251
Not completed	21	11
Consent withdrawn by subject	11	6
Other - adverse event	7	3
Protocol violation	1	-
Lost to follow-up	2	2

Baseline characteristics

Reporting groups	
Reporting group title	ABP 501
Reporting group description:	
Participants received ABP 501 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.	
Reporting group title	Adalimumab
Reporting group description:	
Participants received adalimumab 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.	

Reporting group values	ABP 501	Adalimumab	Total
Number of subjects	264	262	526
Age categorical Units: Subjects			
Adults (18-64 years)	205	197	402
From 65-84 years	59	65	124
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.4	56.3	
standard deviation	± 11.88	± 11.47	-
Gender categorical Units: Subjects			
Female	214	212	426
Male	50	50	100
Race Units: Subjects			
White	251	249	500
Black or African American	9	12	21
Asian	3	0	3
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	1	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	33	25	58
Not Hispanic or Latino	230	236	466
Not Allowed to Collect	1	1	2
Geographic Region Units: Subjects			
Eastern Europe	169	168	337
Western Europe	22	20	42
North America	72	72	144
Latin America	1	2	3
Prior Biological use for RA Units: Subjects			
Yes	71	74	145

No	193	188	381

Duration of RA			
Units: years			
arithmetic mean	9.41	9.37	
standard deviation	± 8.076	± 8.047	-
Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)			
The DAS28-CRP is a composite score to measure disease activity in patients with rheumatoid arthritis, derived from the following variables: • The number of swollen and tender joints assessed using the 28-joint count; • C-reactive protein (CRP) level • Patient's global assessment of disease activity assessed on a score from 0 to 100 transformed from the result measured on a horizontal scale from 0 (no RA activity at all) to 10 (worst RA activity imaginable). The DAS28-CRP score ranges from approximately zero to ten. Higher scores indicate higher disease activity.			
Units: units on a scale			
arithmetic mean	5.66	5.68	
standard deviation	± 0.918	± 0.911	-
Swollen Joint Count			
Sixty-six joints were assessed and classified as swollen/not swollen by pressure and joint manipulation on physical examination.			
Units: joints			
arithmetic mean	14.7	14.1	
standard deviation	± 9.05	± 7.98	-
Tender Joint Count			
Sixty-eight joints were assessed and classified as tender/not tender by pressure and joint manipulation on physical examination.			
Units: joints			
arithmetic mean	24.3	23.9	
standard deviation	± 14.35	± 13.49	-
Subject Global Health Assessment			
The participant's overall assessment of their disease activity in the past week on a 0 to 10 horizontal scale. The left-hand extreme of the scale was described as "no RA activity at all" (symptom-free and no arthritis symptoms; score = 0) and the right-hand extreme as "worst RA activity imaginable" (maximum arthritis disease activity; score = 10).			
Units: units on a scale			
arithmetic mean	6.5	6.6	
standard deviation	± 1.92	± 1.86	-
Investigator Global Health Assessment			
The Investigator's assessment of the participant's current disease activity on a 0 to 10 horizontal scale. The left-hand extreme of the scale was described as "no activity at all" (symptom-free and no arthritis symptoms; score = 0) and the right-hand extreme as "worst activity imaginable" (maximum arthritis disease activity; score = 10).			
Units: units on a scale			
arithmetic mean	6.8	6.7	
standard deviation	± 1.29	± 1.59	-
Subject's assessment of disease related pain			
The subject's assessment of their current level of pain on a 100-mm horizontal visual analogue scale (VAS). The left-hand extreme of the line was described as "no pain at all" (score = 0) and the right-hand extreme as "worst pain imaginable" (score = 100).			
Units: mm			
arithmetic mean	58.3	60.6	
standard deviation	± 21.82	± 22.37	-

Health Assessment Questionnaire-Disability Index (HAQ-DI)			
The HAQ-DI is a questionnaire on which participants are asked to rate their level of difficulty on daily activities (dressing and grooming, arising, eating, and walking) and personal abilities (hygiene, reach, grip, and activity) as well as their use of aids, devices, or help from another person for these activities and disabilities. Responses are scored from 0 indicating no difficulty to 3 indicating inability to perform a task in that area. The overall score is the average of each of the 8 category scores and ranges from 0 (no disability) to 3 (very severe, high-dependency disability).			
Units: units on a scale			
arithmetic mean	1.4819	1.4976	
standard deviation	± 0.61715	± 0.64743	-
C-reactive Protein			
Units: mg/L			
arithmetic mean	13.881	14.678	
standard deviation	± 20.687	± 19.3848	-

End points

End points reporting groups

Reporting group title	ABP 501
Reporting group description:	
Participants received ABP 501 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.	
Reporting group title	Adalimumab
Reporting group description:	
Participants received adalimumab 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.	

Primary: Percentage of Participants with an American College of Rheumatology (ACR) 20 Response at Week 24

End point title	Percentage of Participants with an American College of Rheumatology (ACR) 20 Response at Week 24

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
- ≥ 20% improvement in tender joint count;
- ≥ 20% improvement in swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Subject's assessment of pain (measured on a 100 mm VAS);
  - Subject's Global Health Assessment (measured on a horizontal scale from 0 to 10);
  - Investigator's Global Health Assessment (measured on a horizontal scale from 0 to 10);
  - Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
  - C-reactive protein level.

For the primary analysis based on the full analysis set (all randomized participants), missing values were imputed using the last observation carried forward (LOCF) method.

End point type	Primary
End point timeframe:	
Baseline and Week 24	

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264[1]	262[2]		
Units: percentage of participants				
number (not applicable)	74.6	72.4		

Notes:

[1] - Participants who were randomized and had at least 1 post-baseline assessment up to Week 24 (n = 260)

[2] - Participants who were randomized and had at least 1 post-baseline assessment up to Week 24 (n = 261)

Statistical analyses

Statistical analysis title	Analysis of ACR20 at Week 24

Statistical analysis description:

Clinical equivalence for the primary endpoint, the risk ratio (RR) of ACR20 at week 24, was evaluated by comparing the 2-sided 90% confidence interval (CI) of the RR of ACR20 between ABP 501 and

adalimumab with an equivalence margin of (0.738, 1/0.738). The 90% CI was estimated using a generalized linear model (specifically, a log-binomial regression model), adjusted for geographic region and prior biological use for RA as covariates in the model.

Comparison groups	ABP 501 v Adalimumab
Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk ratio (RR)
Point estimate	1.039
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.954
upper limit	1.133

Secondary: Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)

End point title	Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)

End point description:

The DAS28-CRP is a composite score to measure disease activity in patients with rheumatoid arthritis, derived from the following variables:
• The number of swollen and tender joints assessed using the 28-joint count;
• C-reactive protein (CRP) level
• Patient's global assessment of disease activity assessed on a score from 0 to 100 transformed from the result measured on a horizontal scale from 0 (no RA activity at all) to 10 (worst RA activity imaginable).

The DAS28-CRP score ranges from approximately zero to ten. Higher DAS28-CRP scores indicate higher disease activity.
A repeated measures analysis with the DAS28-CRP change from baseline as the response and the stratification variables, visit, treatment, treatment-by-visit interaction and the baseline DAS28-CRP measurement as predictors in the model was performed.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12, 18, and 24

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264[3]	262[4]		
Units: units on a scale				
least squares mean (standard deviation)				
Week 2 (n = 254, 252)	-1.01 (± 0.891)	-0.96 (± 0.89)		
Week 4 (n = 255, 254)	-1.45 (± 1.048)	-1.42 (± 0.979)		
Week 8 (n = 247, 255)	-1.79 (± 1.075)	-1.7 (± 1.093)		
Week 12 (n = 245, 250)	-2.04 (± 1.112)	-1.93 (± 1.171)		
Week 18 (n = 244, 250)	-2.3 (± 1.184)	-2.17 (± 1.189)		

Week 24 (n = 243, 250)	-2.32 (± 1.237)	-2.32 (± 1.209)		

Notes:

[3] - Full analysis set with available data at each time point

[4] - Full analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an ACR20 Response at Week 2 and Week 8

End point title	Percentage of Participants with an ACR20 Response at Week 2 and Week 8

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
- ≥ 20% improvement in tender joint count;
- ≥ 20% improvement in swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Subject's assessment of pain (measured on a 100 mm VAS);
  - Subject's Global Health Assessment (measured on a horizontal scale from 0 to 10);
  - Investigator's Global Health Assessment (measured on a horizontal scale from 0 to 10);
  - Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
  - C-reactive protein level.

End point type	Secondary

End point timeframe:

Baseline and weeks 2 and 8

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264[5]	262[6]		
Units: percentage of participants				
number (not applicable)				
Week 2 (n = 254, 257)	35.4	24.5		
Week 8 (n = 260, 261)	63.5	62.5		

Notes:

[5] - Full analysis set with LOCF

[6] - Full analysis set with LOCF

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an ACR50 Response at Week 24

End point title	Percentage of Participants with an ACR50 Response at Week 24

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
- ≥ 50% improvement in tender joint count;
- ≥ 50% improvement in swollen joint count; and
- ≥ 50% improvement in at least 3 of the 5 following parameters:
  - Subject's assessment of pain (measured on a 100 mm VAS);

◦ Subject's Global Health Assessment (measured on a horizontal scale from 0 to 10);
◦ Investigator's Global Health Assessment (measured on a horizontal scale from 0 to 10);
◦ Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
◦ C-reactive protein level.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[7]	252[8]		
Units: percentage of participants				
number (not applicable)	49.2	52		

Notes:

[7] - Full analysis set with available data

[8] - Full analysis set with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an ACR70 Response at Week 24

End point title	Percentage of Participants with an ACR70 Response at Week 24

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
• ≥ 70% improvement in tender joint count;
• ≥ 70% improvement in swollen joint count; and
• ≥ 70% improvement in at least 3 of the 5 following parameters:
◦ Subject's assessment of pain (measured on a 100 mm VAS);
◦ Subject's Global Health Assessment (measured on a horizontal scale from 0 to 10);
◦ Investigator's Global Health Assessment (measured on a horizontal scale from 0 to 10);
◦ Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
◦ C-reactive protein level.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[9]	253[10]		
Units: percentage of participants				
number (not applicable)	26	22.9		

Notes:

[9] - Full analysis set with available data

[10] - Full analysis set with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events

End point description:

Adverse events (AEs) were graded for severity according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 according to the following scale:
1 = mild; 2 = moderate; 3 = severe; 4 = life-threatening; 5 = fatal.
A treatment-related AE is defined as an event where the answer to the question "is there a reasonable possibility that the event may have been caused by the Investigational Medicinal Product" was yes.
A serious adverse event is defined as an AE that meets at least 1 of the following serious criteria:
• fatal
• life threatening (places the subject at immediate risk of death)
• requires inpatient hospitalization or prolongation of existing hospitalization
• results in persistent or significant disability/incapacity
• congenital anomaly/birth defect
• other medically important serious event.

End point type	Secondary

End point timeframe:

From the time of first treatment up to 28 days following the last dose of study treatment; 26 weeks.

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: participants				
Any adverse event	132	143		
Adverse event ≥ grade 3	9	17		
Treatment-related adverse event	50	56		
Treatment-related adverse event ≥ grade 3	3	2		
Serious adverse event	10	13		
AE leading to discontinuation of study drug	5	2		
TRAE leading to discontinuation of study drug	4	1		
AE leading to discontinuation from study	7	2		
TRAE leading to discontinuation from study	5	0		
Treatment-related serious adverse event	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Developed Antibodies to ABP 501 or Adalimumab

End point title	Percentage of Participants Who Developed Antibodies to ABP 501 or Adalimumab

End point description:

Two validated assays were used to detect the presence of anti-drug antibodies. Samples were first tested in an electrochemiluminescence (ECL)-based bridging immunoassay to detect anti-drug antibodies (ADA) against ABP 501 and adalimumab (Binding Antibody Assay). Samples confirmed to be positive for binding antibodies were subsequently tested in a non-cell based bioassay to determine neutralizing activity against ABP 501 or adalimumab (Neutralizing Antibody Assay).
Developing antibody incidence is defined as a negative or no antibody result at baseline and a positive antibody result at a post-baseline time point.

End point type	Secondary

End point timeframe:

Up to week 26

End point values	ABP 501	Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264[11]	262[12]		
Units: percentage of participants				
number (not applicable)				
Developing Binding Antibody	38.3	38.2		
Developing Neutralizing Antibody	9.1	11.1		

Notes:

[11] - Participants with at least 1 evaluable antibody test result (to either ABP 501 or adalimumab)

[12] - Participants with at least 1 evaluable antibody test result (to either ABP 501 or adalimumab)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of first treatment but on or within 28 days following the last dose of study treatment; 26 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	ABP 501

Reporting group description:

Participants received ABP 501 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.

Reporting group title	Adalimumab

Reporting group description:

Participants received adalimumab 40 mg subcutaneously on day 1 and every 2 weeks thereafter until week 22.

Serious adverse events	ABP 501	Adalimumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 264 (3.79%)	13 / 262 (4.96%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Corneal graft rejection			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			

subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 264 (0.38%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 264 (0.00%)	1 / 262 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 264 (0.76%)	0 / 262 (0.00%)	
occurrences causally related to treatment / all	2 / 2	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 501	Adalimumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 264 (6.44%)	19 / 262 (7.25%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 264 (6.44%)	19 / 262 (7.25%)	
occurrences (all)	19	21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 June 2013	• changed the primary endpoint to RR of ACR20 at week 24 (assuming an expected ACR20 response for both ABP 501 and adalimumab of 63% at week 24) between ABP 501 and adalimumab, with an equivalence margin of (0.738, 1/0.738) • changed the secondary efficacy criteria to the following: o DAS28-CRP change from baseline at weeks 2, 4, 8, 12, 18, and 24 o RR of ACR20 at weeks 2 and 8 o RR of ACR50 and ACR70 responses at week 24 • added efficacy assessments at weeks 2, 8, and 18 to support the secondary criteria • required study discontinuation in the case of pregnancy and removed the requirement for discontinuation for progressive disease • changed the Subject and Investigator Global Health Assessments to 0 to 10 horizontal scale (rather than VAS) and updated the description of the pain VAS to match the sample form

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported