



Clinical trial results:

A Phase 2 Study to Investigate the Safety and Efficacy of ABT-122 Given with Methotrexate in Subjects with Active Rheumatoid Arthritis Who Have an Inadequate Response to Methotrexate

Summary

EudraCT number	2013-004019-37
Trial protocol	DE HU BG CZ DK RO
Global end of trial date	01 October 2015

Results information

Result version number	v1
This version publication date	26 November 2016
First version publication date	26 November 2016

Trial information

Trial identification

Sponsor protocol code	M12-963
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02141997
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Information, AbbVie, 001 00-633-9110,
Scientific contact	Heikki Mansikka, MD, AbbVie, heikki.mansikka@abbvie.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	01 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is a Phase 2 randomized, double-blind, double-dummy, parallel-group study designed to assess the safety, tolerability, efficacy, pharmacokinetics and immunogenicity of multiple doses of ABT 122 in subjects with active rheumatoid arthritis (RA) who are inadequately responding to methotrexate (MTX) treatment.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2014
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	Bulgaria: 17
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Poland: 112
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	United States: 49
Worldwide total number of subjects	222
EEA total number of subjects	164

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)	169
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a 30-day screening period.

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, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Adalimumab 40 mg EOW
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Arm description:

Adalimumab 40 mg every other week (EOW) for 11 weeks.

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:

adalimumab administered as subcutaneous injection every other week (EOW)

Arm title	ABT-122 60 mg EOW
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Arm description:

ABT-122 60 mg every other week (EOW) for 11 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ABT-122 administered as subcutaneous injection every other week (EOW)

Arm title	ABT-122 120 mg EOW
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Arm description:

ABT-122 120 mg every other week (EOW) for 11 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ABT-122 administered as subcutaneous injection every other week (EOW)

Arm title	ABT-122 120 mg EW
Arm description: ABT-122 120 mg every week (EW) for 11 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ABT-122 administered as subcutaneous injection every other week (EOW)

Number of subjects in period 1	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW
Started	56	55	56
Completed	53	49	53
Not completed	3	6	3
Adverse event, non-fatal	-	2	-
Not specified	1	4	-
Withdrew consent	1	-	3
Participant noncompliance	1	-	-

Number of subjects in period 1	ABT-122 120 mg EW
Started	55
Completed	54
Not completed	1
Adverse event, non-fatal	1
Not specified	-
Withdrew consent	-
Participant noncompliance	-

Baseline characteristics

Reporting groups

Reporting group title	Adalimumab 40 mg EOW
Reporting group description: Adalimumab 40 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 60 mg EOW
Reporting group description: ABT-122 60 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 120 mg EOW
Reporting group description: ABT-122 120 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 120 mg EW
Reporting group description: ABT-122 120 mg every week (EW) for 11 weeks.	

Reporting group values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW
Number of subjects	56	55	56
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	57.6	55.2	53.5
standard deviation	± 12.36	± 11.81	± 13
Gender, Male/Female Units: participants			
Female	42	45	49
Male	14	10	7

Reporting group values	ABT-122 120 mg EW	Total	
Number of subjects	55	222	
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	55.6		
standard deviation	± 12.34	-	
Gender, Male/Female Units: participants			
Female	45	181	
Male	10	41	

End points

End points reporting groups

Reporting group title	Adalimumab 40 mg EOW
Reporting group description: Adalimumab 40 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 60 mg EOW
Reporting group description: ABT-122 60 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 120 mg EOW
Reporting group description: ABT-122 120 mg every other week (EOW) for 11 weeks.	
Reporting group title	ABT-122 120 mg EW
Reporting group description: ABT-122 120 mg every week (EW) for 11 weeks.	

Primary: Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response at Week 12

End point title	Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response at Week 12
End point description: Response defined as at least 20% reduction (improvement) compared with baseline in tender joint count (TJC68), swollen joint count (SJC66), and at least 3 of the 5 remaining ACR core set measures: patient's assessment of pain, patient's global assessment of disease activity (PtGA); physician's global assessment of disease activity (PGA), Health Assessment Questionnaire – Disability Index (HAQ-DI), and high-sensitivity C-reactive protein (hsCRP). Last observation carried forward (LOCF) was used for missing data (only post-baseline values were carried forward).	
End point type	Primary
End point timeframe: Baseline (Day 1) and Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	73.2	65.5	76.8	81.8

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: P-value calculated using 1-sided Fisher's Exact test.	
Comparison groups	Adalimumab 40 mg EOW v ABT-122 60 mg EOW

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.863
Method	Fisher exact

Statistical analysis title	Statistical analysis 2
Statistical analysis description: P-value calculated using 1-sided Fisher's Exact test.	
Comparison groups	Adalimumab 40 mg EOW v ABT-122 120 mg EOW
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.414
Method	Fisher exact

Statistical analysis title	Statistical analysis 3
Statistical analysis description: P-value calculated using 1-sided Fisher's Exact test.	
Comparison groups	Adalimumab 40 mg EOW v ABT-122 120 mg EW
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.196
Method	Fisher exact

Secondary: Change in Disease Activity Score 28 With High Sensitivity C-Reactive Protein (DAS28 [hsCRP])

End point title	Change in Disease Activity Score 28 With High Sensitivity C-Reactive Protein (DAS28 [hsCRP])
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End point description:

The DAS28 (hsCRP) is a validated index of rheumatoid arthritis disease activity. Twenty-eight tender joint counts, 28 swollen joint counts, hsCRP, and general health are included in the DAS28 (hsCRP) score. Scores range from 0 to 10: a score >5.1 indicates high disease activity, a score <3.2 indicates low disease activity, and a score <2.6 indicates clinical remission. A negative change from baseline represents improvement. n=the number of participants with evaluable data at each time point. LOCF was used (only post-baseline values were carried forward).

End point type	Secondary
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End point timeframe:

Baseline, Weeks 2, 4, 6, 8, and 12

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=54,53,55,53)	-1.43 (-1.71 to -1.15)	-1.26 (-1.54 to -0.97)	-1.8 (-2.08 to -1.52)	-1.69 (-1.97 to -1.41)
Week 4 (n=56,55,56,55)	-1.86 (-2.17 to -1.55)	-1.66 (-1.97 to -1.34)	-2.08 (-2.39 to -1.78)	-2.15 (-2.46 to -1.84)
Week 6 (n=56,55,56,55)	-2.28 (-2.6 to -1.96)	-1.83 (-2.16 to -1.51)	-2.39 (-2.71 to -2.07)	-2.41 (-2.74 to -2.09)
Week 8 (n=56,55,56,55)	-2.32 (-2.64 to -2)	-1.98 (-2.31 to -1.65)	-2.6 (-2.93 to -2.28)	-2.58 (-2.91 to -2.25)
Week 12 (n=56,55,56,55)	-2.44 (-2.75 to -2.12)	-2.06 (-2.38 to -1.74)	-2.64 (-2.95 to -2.33)	-2.67 (-2.98 to -2.35)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response at Week 12

End point title	Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response at Week 12
End point description:	Response defined as at least 50% reduction (improvement) compared with baseline in tender joint count (TJC68), swollen joint count (SJC66), and at least 3 of the 5 remaining ACR core set measures: patient's assessment of pain, PtGA; PGA, HAQ-DI, and hsCRP. LOCF was used (only post-baseline values were carried forward).
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	54
Units: percentage of participants				
number (not applicable)	51.8	34.5	48.2	48.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response at Week 12

End point title	Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response at Week 12
End point description: Response defined as at least 70% reduction (improvement) compared with baseline in tender joint count (TJC68), swollen joint count (SJC66), and at least 3 of the 5 remaining ACR core set measures: patient's assessment of pain, PtGA; PGA, HAQ-DI, and hsCRP. LOCF was used (only post-baseline values were carried forward).	
End point type	Secondary
End point timeframe: Baseline (Day 1) and Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	23.2	23.6	19.6	36.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) or Clinical Remission (CR) Based on DAS28 (hsCRP) at Week 12

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) or Clinical Remission (CR) Based on DAS28 (hsCRP) at Week 12
End point description: The DAS28 (hsCRP) is a validated index of rheumatoid arthritis disease activity. Twenty-eight tender joint counts, 28 swollen joint counts, hsCRP, and general health are included in the DAS28 (hsCRP) score. Scores range from 0 to 10: a score >5.1 indicates high disease activity, a score <3.2 indicates low disease activity, and a score <2.6 indicates clinical remission. LDA is defined as a DAS28 (hsCRP) score from 2.6 to < 3.2 at Week 12. CR is defined as a DAS28 (hsCRP) score < 2.6 at Week 12. LOCF was used (only post-baseline values were carried forward).	
End point type	Secondary
End point timeframe: Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	50	34.5	53.6	54.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving CR based on DAS28 (hsCRP) at Week 12

End point title	Percentage of Participants Achieving CR based on DAS28 (hsCRP) at Week 12
End point description: The DAS28 (hsCRP) is a validated index of rheumatoid arthritis disease activity. Twenty-eight tender joint counts, 28 swollen joint counts, hsCRP, and general health are included in the DAS28 (hsCRP) score. Scores range from 0 to 10: a score >5.1 indicates high disease activity, a score <3.2 indicates low disease activity, and a score <2.6 indicates clinical remission. CR is defined as a DAS28 (hsCRP) score < 2.6 at Week 12. LOCF was used (only post-baseline values were carried forward).	
End point type	Secondary
End point timeframe: Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	32.1	23.6	39.3	41.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving LDA or CR Based on Clinical Disease Activity Index (CDAI) at Week 12

End point title	Percentage of Participants Achieving LDA or CR Based on Clinical Disease Activity Index (CDAI) at Week 12
End point description: The clinical disease activity index (CDAI) is a composite index for assessing disease activity based on the summation of the counts of TJC28 and SJC28, patient global assessment of disease activity measured on a VAS from 0 to 10 cm, and physician global assessment of disease activity measured on a VAS from 0 to 10 cm. The total CDAI score ranges from 0 to 78 with higher scores indicating higher disease activity. LDA is defined as a CDAI score from 2.8 to ≤ 10 at Week 12. CR is defined as a CDAI score ≤ 2.8 at Week 12. LOCF was used (only post-baseline values were carried forward).	
End point type	Secondary
End point timeframe: Week 12	

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	42.9	36.4	44.6	54.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving CR Based on Clinical Disease Activity Index (CDAI) at Week 12

End point title	Percentage of Participants Achieving CR Based on Clinical Disease Activity Index (CDAI) at Week 12
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End point description:

The clinical disease activity index (CDAI) is a composite index for assessing disease activity based on the summation of the counts of TJC28 and SJC28, patient global assessment of disease activity measured on a VAS from 0 to 10 cm, and physician global assessment of disease activity measured on a VAS from 0 to 10 cm. The total CDAI score ranges from 0 to 78 with higher scores indicating higher disease activity. CR is defined as a CDAI score \leq 2.8 at Week 12. LOCF was used (only post-baseline values were carried forward).

End point type	Secondary
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End point timeframe:

Week 12

End point values	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW	ABT-122 120 mg EW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	55
Units: percentage of participants				
number (not applicable)	8.9	7.3	10.7	10.9

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 21 weeks); serious adverse events (SAEs) were collected from the time informed consent was obtained (25 weeks).

Adverse event reporting additional description:

A TEAE is defined as any AE with onset or worsening reported by a subject from the time that the first dose of study drug is administered until 70 days have elapsed following discontinuation of study drug administration. TEAEs were collected whether elicited or spontaneously reported by the subject.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Adalimumab 40 mg EOW
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Reporting group description:

Adalimumab 40 mg every other week (EOW) for 11 weeks.

Reporting group title	ABT-122 60 mg EOW
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Reporting group description:

ABT-122 60 mg every other week (EOW) for 11 weeks.

Reporting group title	ABT-122 120 mg EOW
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Reporting group description:

ABT-122 120 mg every other week (EOW) for 11 weeks.

Reporting group title	ABT-122 120 mg EW
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Reporting group description:

ABT-122 120 mg every week (EW) for 11 weeks.

Serious adverse events	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	0 / 56 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 56 (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
Tibia fracture			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 56 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 56 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 56 (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

Serious adverse events	ABT-122 120 mg EW		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 55 (3.64%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Ovarian cyst			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adalimumab 40 mg EOW	ABT-122 60 mg EOW	ABT-122 120 mg EOW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 56 (21.43%)	11 / 55 (20.00%)	11 / 56 (19.64%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	3 / 56 (5.36%)
occurrences (all)	0	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	3 / 56 (5.36%)
occurrences (all)	0	0	3
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 56 (3.57%)	1 / 55 (1.82%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	2 / 56 (3.57%)
occurrences (all)	0	4	2
Somnolence			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 56 (3.57%)	3 / 55 (5.45%)	0 / 56 (0.00%)
occurrences (all)	2	4	0

Nausea subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2	0 / 55 (0.00%) 0	0 / 56 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2	0 / 55 (0.00%) 0	0 / 56 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0	0 / 55 (0.00%) 0	2 / 56 (3.57%) 3
Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0 3 / 56 (5.36%) 3 1 / 56 (1.79%) 1 1 / 56 (1.79%) 1	0 / 55 (0.00%) 0 2 / 55 (3.64%) 2 1 / 55 (1.82%) 1 5 / 55 (9.09%) 7	2 / 56 (3.57%) 2 1 / 56 (1.79%) 1 0 / 56 (0.00%) 0 1 / 56 (1.79%) 1

Non-serious adverse events	ABT-122 120 mg EW		
Total subjects affected by non-serious adverse events subjects affected / exposed	10 / 55 (18.18%)		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0 0 / 55 (0.00%) 0		
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1 0 / 55 (0.00%) 0		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1 0 / 55 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection	2 / 55 (3.64%) 2 3 / 55 (5.45%) 3		

subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 April 2014	The purpose of this amendment was to remove Part 2 Open-label Extension (OLE) Period to separate the randomized control trial and the OLE trial into 2 protocols; remove pharmacokinetics sub-study and revise pharmacokinetics analyses; clarify that re-screening was permitted only once per subject; and revise inclusion (remove body mass index) and exclusion criteria (clarify HCV testing and chest x-ray requirements).
13 February 2015	The purpose of this amendment was to clarify lab retesting requirements and window visits; revise study site numbers to at least 85 sites globally; update female and male reproductive language; and update inclusion (high sensitivity C-reactive protein [hsCRP] criteria or positive rheumatoid factor [RF] and anticyclic citrullinated peptide [anti-CCP] antibody levels) and exclusion criteria (live vaccinations); remove 24-hour methylhistamine laboratory test; clarify chest x-ray assessment; add injection site reaction language; and revise unblinding for interim analysis;
29 July 2015	The purpose of this amendment was to increase the number of randomized subjects from approximately 160 to approximately 225; add new standard medical and non-medical complaint language; and clarify who could be unblinded for analyses during the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported