Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study to investigate the Safety and Efficacy of ABT-494 Given with Methotrexate (MTX) in Subjects with Moderately to Severely Active Rheumatoid Arthritis (RA) Who Have Had an Inadequate Response or Intolerance to Anti-TNF Biologic Therapy

Summary

EudraCT number	2013-002358-57
Trial protocol	ES CZ HU NL BE
Global end of trial date	27 July 2015

Results information

Result version number	v1
This version publication date	06 August 2016
First version publication date	06 August 2016

Trial information

Trial identification

Sponsor protocol code	M13-550

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01960855
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 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Steven Jungerwirth, MD, AbbVie, steven.jungerwirth@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	27 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the safety and efficacy of multiple doses of ABT-494 versus placebo in moderately to severely active RA subjects on stable background MTX therapy with inadequate response or intolerance to anti-TNF biologic therapy.

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	31 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: 33
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Puerto Rico: 11
Country: Number of subjects enrolled	United States: 176
Worldwide total number of subjects	276
EEA total number of subjects	83

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)	196
From 65 to 84 years	78
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a screening period of 30 days.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo BID

Arm description:

Placebo twice daily (BID) for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo for ABT-494 capsule administered orally twice daily (BID).

Arm title	ABT-494 3 mg BID

Arm description:

ABT-494 3 mg twice daily (BID) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-494
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

ABT-494 capsule administered orally twice daily (BID).

Arm title	ABT-494 6 mg BID

Arm description:

ABT-494 6 mg twice daily (BID) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-494
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

ABT-494 capsule administered orally twice daily (BID).

Arm title	ABT-494 12 mg BID
Arm description:	
ABT-494 12 mg twice daily (BID) for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-494
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
ABT-494 capsule administered orally twice daily (BID).	

Arm title	ABT-494 18 mg BID
Arm description:	
ABT-494 18 mg twice daily (BID) for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-494
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
ABT-494 capsule administered orally twice daily (BID).	

Number of subjects in period 1	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID
Started	56	55	55
Completed	45	51	46
Not completed	11	4	9
Consent withdrawn by subject	3	1	2
Not specified	2	1	1
Adverse event	2	-	6
Lost to follow-up	2	1	-
Subject noncompliant	1	-	-
Lack of efficacy	1	1	-

Number of subjects in period 1	ABT-494 12 mg BID	ABT-494 18 mg BID
Started	55	55
Completed	51	50
Not completed	4	5
Consent withdrawn by subject	1	1
Not specified	1	-
Adverse event	2	2
Lost to follow-up	-	2
Subject noncompliant	-	-

Lack of efficacy	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo BID
Reporting group description:	
Placebo twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 3 mg BID
Reporting group description:	
ABT-494 3 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 6 mg BID
Reporting group description:	
ABT-494 6 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 12 mg BID
Reporting group description:	
ABT-494 12 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 18 mg BID
Reporting group description:	
ABT-494 18 mg twice daily (BID) for 12 weeks.	

Reporting group values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID
Number of subjects	56	55	55
Age categorical Units: Subjects			

Age continuous			
Modified intent-to-treat (mITT) population, defined as all randomized subjects who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	57.5	57	56.3
standard deviation	± 12.04	± 13.06	± 11.71
Gender categorical			
mITT population.			
Units: Subjects			
Female	48	43	43
Male	8	12	12

Reporting group values	ABT-494 12 mg BID	ABT-494 18 mg BID	Total
Number of subjects	55	55	276
Age categorical Units: Subjects			

Age continuous			
Modified intent-to-treat (mITT) population, defined as all randomized subjects who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	59.1	56.7	
standard deviation	± 11.4	± 12.39	-

Gender categorical			
mITT population.			
Units: Subjects			
Female	45	42	221
Male	10	13	55

End points

End points reporting groups

Reporting group title	Placebo BID
Reporting group description: Placebo twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 3 mg BID
Reporting group description: ABT-494 3 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 6 mg BID
Reporting group description: ABT-494 6 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 12 mg BID
Reporting group description: ABT-494 12 mg twice daily (BID) for 12 weeks.	
Reporting group title	ABT-494 18 mg BID
Reporting group description: ABT-494 18 mg twice daily (BID) for 12 weeks.	

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

End point title	Number of Subjects 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 (hs CRP). Last observation carried forward (LOCF) was used for missing data.	
End point type	Primary
End point timeframe: Baseline (Week 0) and Week 12	

End point values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID	ABT-494 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54[1]	54[2]	52[3]	55[4]
Units: subjects	19	30	33	40

Notes:

[1] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[2] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[3] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[4] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

End point values	ABT-494 18 mg BID			

Subject group type	Reporting group			
Number of subjects analysed	55[5]			
Units: subjects	39			

Notes:

[5] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo BID v ABT-494 3 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	Chi-squared

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo BID v ABT-494 6 mg BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Chi-squared

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo BID v ABT-494 12 mg BID
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo BID v ABT-494 18 mg BID
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Secondary: Number of Subjects Achieving American College of Rheumatology 50%

(ACR50) Response at Week 12

End point title	Number of Subjects 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 hs CRP. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Week 12

End point values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID	ABT-494 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[6]	54[7]	52[8]	55[9]
Units: subjects	9	13	20	24

Notes:

[6] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[7] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[8] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[9] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

End point values	ABT-494 18 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	55[10]			
Units: subjects	22			

Notes:

[10] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo BID v ABT-494 3 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.364
Method	Chi-squared

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo BID v ABT-494 6 mg BID

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.014
Method	Chi-squared

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo BID v ABT-494 12 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Chi-squared

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo BID v ABT-494 18 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	Chi-squared

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

End point title	Number of Subjects 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 hs CRP. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Week 12

End point values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID	ABT-494 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55[11]	54[12]	52[13]	55[14]
Units: subjects	2	7	14	12

Notes:

[11] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[12] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value
[13] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value
[14] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

End point values	ABT-494 18 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	55[15]			
Units: subjects	12			

Notes:
[15] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo BID v ABT-494 3 mg BID
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.093
Method	Chi-squared

Statistical analysis title	Statistical analysis 2
Comparison groups	ABT-494 6 mg BID v Placebo BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo BID v ABT-494 12 mg BID
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Chi-squared

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo BID v ABT-494 18 mg BID

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Chi-squared

Secondary: Number of Subjects Achieving Low Disease Activity (LDA) Based on Disease Activity Score (DAS28) or Clinical Remission (CR) based on (DAS28) at Week 12

End point title	Number of Subjects Achieving Low Disease Activity (LDA) Based on Disease Activity Score (DAS28) or Clinical Remission (CR) based on (DAS28) at Week 12

End point description:

LDA is defined as DAS28 from 2.6 to < 3.2 at Week 12. CR is defined as DAS28 (CRP) < 2.6 at Week 12. The DAS28 is a validated index of rheumatoid arthritis disease activity. Twenty-eight tender joint counts, 28 swollen joint counts, hs CRP, and general health are included in the DAS28 score. Scores on the DAS28 range from 0 to 10. A DAS28 score >5.1 indicates high disease activity, a DAS28 score <3.2 indicates low disease activity, and a DAS28 score <2.6 indicates clinical remission. LOCF was used.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID	ABT-494 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55[16]	54[17]	53[18]	55[19]
Units: subjects	14	18	20	29

Notes:

[16] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[17] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[18] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[19] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

End point values	ABT-494 18 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	55[20]			
Units: subjects	25			

Notes:

[20] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo BID v ABT-494 3 mg BID

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.366
Method	Chi-squared

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo BID v ABT-494 6 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.17
Method	Chi-squared

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo BID v ABT-494 12 mg BID
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Chi-squared

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo BID v ABT-494 18 mg BID
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.028
Method	Chi-squared

Secondary: Number of Subjects Achieving CR based on DAS28 at Week 12

End point title	Number of Subjects Achieving CR based on DAS28 at Week 12

End point description:

The DAS28 is a validated index of rheumatoid arthritis disease activity. Twenty-eight tender joint counts, 28 swollen joint counts, hs CRP, and general health are included in the DAS28 score. Scores on the DAS28 range from 0 to 10. A DAS28 score >5.1 indicates high disease activity, a DAS28 score <3.2 indicates low disease activity, and a DAS28 score <2.6 indicates clinical remission. LOCF was used.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID	ABT-494 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55[21]	54[22]	53[23]	55[24]
Units: subjects	7	13	14	18

Notes:

[21] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[22] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[23] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

[24] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

End point values	ABT-494 18 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	55[25]			
Units: subjects	17			

Notes:

[25] - Subjects in the mITT population with a baseline value and at least 1 post-baseline value

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo BID v ABT-494 3 mg BID
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.126
Method	Chi-squared

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo BID v ABT-494 6 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.072
Method	Chi-squared

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo BID v ABT-494 12 mg BID

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.012
Method	Chi-squared

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo BID v ABT-494 18 mg BID
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.021
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs (TEAEs) were collected from first dose of study drug until up to 30 days after discontinuation of study drug (up to 16 weeks); SAEs were collected from the time informed consent was obtained (20 weeks).

Adverse event reporting additional description:

A treatment-emergent AE (TEAE) is defined as any AE with onset or worsening reported by a participant from the time that the first dose of study drug is administered 30 days have elapsed following discontinuation of study drug administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo BID

Reporting group description:

Placebo twice daily (BID) for 12 weeks.

Reporting group title	ABT-494 3 mg BID

Reporting group description:

ABT-494 3 mg twice daily (BID) for 12 weeks.

Reporting group title	ABT-494 6 mg BID

Reporting group description:

ABT-494 6 mg twice daily (BID) for 12 weeks.

Reporting group title	ABT-494 12 mg BID

Reporting group description:

ABT-494 12 mg twice daily (BID) for 12 weeks.

Reporting group title	ABT-494 18 mg BID

Reporting group description:

ABT-494 18 mg twice daily (BID) for 12 weeks.

Serious adverse events	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	2 / 55 (3.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
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			
Pancreatitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 55 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
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			
Acute respiratory failure			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (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
Bronchiectasis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ABT-494 12 mg BID	ABT-494 18 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (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			
Transient ischaemic attack			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (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	Placebo BID	ABT-494 3 mg BID	ABT-494 6 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 56 (16.07%)	13 / 55 (23.64%)	13 / 55 (23.64%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	3 / 55 (5.45%)
occurrences (all)	2	3	4
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	1 / 56 (1.79%)	4 / 55 (7.27%)	1 / 55 (1.82%)
occurrences (all)	1	4	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	0 / 55 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	0 / 55 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	0 / 55 (0.00%)
occurrences (all)	3	3	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	1 / 55 (1.82%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	2 / 56 (3.57%)	2 / 55 (3.64%)	1 / 55 (1.82%)
occurrences (all)	2	2	1
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2

Non-serious adverse events	ABT-494 12 mg BID	ABT-494 18 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 55 (25.45%)	27 / 55 (49.09%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 55 (0.00%)	5 / 55 (9.09%)	
occurrences (all)	0	5	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 55 (5.45%)	3 / 55 (5.45%)	
occurrences (all)	4	6	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 55 (5.45%)	1 / 55 (1.82%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 55 (0.00%)	4 / 55 (7.27%)	
occurrences (all)	0	5	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	0 / 55 (0.00%)	4 / 55 (7.27%)	
occurrences (all)	0	7	
Nausea			
subjects affected / exposed	2 / 55 (3.64%)	4 / 55 (7.27%)	
occurrences (all)	3	4	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	4	
Sinusitis			
subjects affected / exposed	1 / 55 (1.82%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	4 / 55 (7.27%)	4 / 55 (7.27%)	
occurrences (all)	5	4	
Urinary tract infection			
subjects affected / exposed	2 / 55 (3.64%)	7 / 55 (12.73%)	
occurrences (all)	2	9	
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	1 / 55 (1.82%)	3 / 55 (5.45%)	
occurrences (all)	1	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2013	The purpose of this amendment is to update inclusion (including RA diagnosis criteria, prior biologic use, hsCRP <ULN criteria, and permitted medications) and exclusion criteria (including live vaccinations, laboratory values, and prohibited medications and therapies), and update study procedures (including chest x-ray permitted at any time per investigator decision, TB tests, and clinical lab tests).
18 November 2014	The purpose of this amendment was to increase the number of sites expected to participate in the study, add and internal independent safety data review committee, add an interim analysis of efficacy, and clarify inclusion (including prior treatment, prohibited and acceptable concomitant medications), clarify study procedures (including blood samples for pharmacokinetics), and clarify patient rollover into open label extension.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported