Clinical trial results:
A Phase 2, Multicenter, Open-Label Extension (OLE) Study with ABT-122 in Active Psoriatic Arthritis Subjects Who Have Completed a Preceding Study M14-197 Phase 2 Randomized Controlled Trial (RCT)

Summary

EudraCT number	2014-005527-27
Trial protocol	HU CZ DE LV ES IT
Global end of trial date	02 August 2016

Results information

Result version number	v1 (current)
This version publication date	11 June 2017
First version publication date	11 June 2017

Trial information

Trial identification

Sponsor protocol code	M14-198

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02429895
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Lawrence McNamee, Program Lead, AbbVie, lawrence.mcnamee@abbvie.com
Scientific contact	Peloso, Paul, Medical Director, AbbVie, paul.peloso@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	02 August 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Assess the long term efficacy, and safety and tolerability of ABT-122 in psoriatic arthritis (PsA) subjects on background methotrexate (MTX) who have completed Study M14-197, a Phase 2 randomized controlled trial (RCT).

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 89
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Bulgaria: 30
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Latvia: 22
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	New Zealand: 5
Worldwide total number of subjects	168
EEA total number of subjects	161

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)	151
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 168 subjects diagnosed with active RA on background MTX who had participated in the RCT Study M14-197 (2014-003558-15) enrolled in this open-label extension (OLE).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ABT-122

Arm description:

Open-label ABT-122 240 mg every other week (EOW) for 24 weeks

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

Dosage and administration details:

All subjects were treated with ABT-122 240 mg EOW in an open-label fashion with the possibility of an extra 240 mg dose. In order to be considered for the extra dose the subject must have met American College of Rheumatology (ACR) 20 response criteria in the RCT (Study M14-197) or in the OLE (Study M14-198) and afterward lost ACR20 response.

Number of subjects in period 1	ABT-122
Started	168
Completed	29
Not completed	139
Subject noncompliance	1
Consent withdrawn by subject	5
Study termination	129
Adverse event	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	168	168	
Age categorical Units: Subjects			
< 40 years	48	48	
40 to < 65 years	103	103	
>= 65 years	17	17	
Age continuous Units: years			
arithmetic mean	47.7		
standard deviation	± 12.66	-	
Gender categorical Units: Subjects			
Female	81	81	
Male	87	87	

End points

End points reporting groups

Reporting group title	ABT-122
Reporting group description:	
Open-label ABT-122 240 mg every other week (EOW) for 24 weeks	

Primary: ACR20 Response Rate by Visit

End point title	ACR20 Response Rate by Visit[1]

End point description:

Percentage of subjects with an ACR20 response, defined as at least 20% improvement (compared to baseline values) in tender and swollen joint counts and at least 20% improvement in 3 of the remaining 5 core set measures (subject global assessment of pain, subject global assessment of disease activity, physician global assessment of disease activity, subject assessment of physical function and acute phase reactant high sensitivity C-reactive protein [hsCRP]). Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Primary

End point timeframe:

Weeks 4, 8, 16, 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics, along with 95% confidence intervals, are presented per protocol.

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=163	76.7 (69.6 to 82.5)			
Week 8; n=158	79.7 (72.8 to 85.3)			
Week 16; n=117	81.2 (73.1 to 87.3)			
Week 24; n=45	77.8 (63.5 to 87.6)			

Statistical analyses

No statistical analyses for this end point

Primary: ACR50 Response Rate by Visit

End point title	ACR50 Response Rate by Visit[2]

End point description:

Percentage of subjects with an ACR50 response, defined as at least 50% improvement (compared to baseline values) in tender and swollen joint counts and at least 50% improvement in 3 of the remaining

5 core set measures (subject global assessment of pain, subject global assessment of disease activity, physician global assessment of disease activity, subject assessment of physical function and acute phase reactant hsCRP). Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Primary

End point timeframe:

Weeks 4, 8, 16, 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics, along with 95% confidence intervals, are presented per protocol.

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=165	48.5 (41 to 56.1)			
Week 8; n=159	45.3 (37.7 to 53)			
Week 16; n=118	48.3 (39.5 to 57.2)			
Week 24; n=46	50 (36.1 to 63.9)			

Statistical analyses

No statistical analyses for this end point

Primary: ACR70 Response Rate by Visit

End point title	ACR70 Response Rate by Visit[3]

End point description:

Percentage of subjects with an ACR70 response, defined as at least 70% improvement (compared to baseline values) in tender and swollen joint counts and at least 70% improvement in 3 of the remaining 5 core set measures (subject global assessment of pain, subject global assessment of disease activity, physician global assessment of disease activity, subject assessment of physical function and acute phase reactant hsCRP). Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Primary

End point timeframe:

Weeks 4, 8, 16, 24

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics, along with 95% confidence intervals, are presented per protocol.

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=165	23.6 (17.8 to 30.7)			
Week 8; n=159	27 (20.7 to 34.5)			
Week 16; n=118	29.7 (22.1 to 38.5)			
Week 24; n=46	26.1 (15.5 to 40.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Disease Activity Score 28 (DAS28[hsCRP]) by Visit

End point title	Change from Baseline in Disease Activity Score 28 (DAS28[hsCRP]) by Visit

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, with higher scores indicating more disease activity.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n= subjects available at both the given visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=162	-2.12 (± 1.211)			
Week 8; n=159	-2.18 (± 1.26)			
Week 16; n=118	-2.21 (± 1.27)			
Week 24; n=45	-2.09 (± 1.036)			

Statistical analyses

No statistical analyses for this end point

Secondary: Low Disease Activity (LDA) or Clinical Remission (CR) Response Rate per DAS28 (hsCRP) by Visit

End point title	Low Disease Activity (LDA) or Clinical Remission (CR) Response Rate per DAS28 (hsCRP) by Visit

End point description:

Percentage of subjects achieving LDA or CR on the DAS28 (hsCRP). 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, with higher scores indicating more disease activity. LDA was defined as a score from 2.6 to < 3.2, and CR was defined as a score < 2.6. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n= subjects available at both the given visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=162	64.2 (56.6 to 71.2)			
Week 8; n=159	69.8 (62.3 to 76.4)			
Week 16; n=118	71.2 (62.4 to 78.6)			
Week 24; n=45	84.4 (70.9 to 92.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: CR Response Rate Per DAS28 (hsCRP) by Visit

End point title	CR Response Rate Per DAS28 (hsCRP) by Visit

End point description:

Percentage of subjects achieving CR on the DAS28 (hsCRP). 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, with higher scores indicating more disease activity. CR was defined as a score < 2.6. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n= subjects available at both the given visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 32

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=162	43.8 (36.4 to 51.5)			
Week 8; n=159	46.5 (39 to 54.3)			
Week 16; n=118	51.7 (42.8 to 60.5)			
Week 24; n=45	64.4 (49.8 to 76.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Area and Severity Index (PASI) 50 Response Rate by Visit

End point title	Psoriasis Area and Severity Index (PASI) 50 Response Rate by Visit

End point description:

Percentage of PASI50 responders, defined as a 50% improvement in PASI score compared to baseline in subjects with ≥ 3% Body Surface Area (BSA) psoriasis involvement at baseline. PASI assesses four anatomic sites (head, upper extremities, trunk, and lower extremities) for erythema, induration and desquamation related to psoriasis. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest possible degree. Typically, scores of 3 or less represent mild disease, scores over 3 and up and including 15 represent moderate disease, and scores over 15 are considered to be associated with severe disease. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=93	91.4 (83.7 to 95.8)			

Week 8; n=86	91.9 (83.9 to 96.3)			
Week 16; n=64	90.6 (80.7 to 96)			
Week 24; n=23	100 (83.1 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: PASI75 Response Rate by Visit

End point title	PASI75 Response Rate by Visit

End point description:

Percentage of PASI75 responders, defined as a 75% improvement in PASI score compared to baseline in subjects with ≥ 3% BSA psoriasis involvement at baseline. PASI assesses four anatomic sites (head, upper extremities, trunk, and lower extremities) for erythema, induration and desquamation related to psoriasis. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest possible degree. Typically, scores of 3 or less represent mild disease, scores over 3 and up and including 15 represent moderate disease, and scores over 15 are considered to be associated with severe disease. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=93	78.5 (69 to 85.7)			
Week 8; n=86	77.9 (68 to 85.5)			
Week 16; n=64	84.4 (73.4 to 91.5)			
Week 24; n=23	82.6 (62.3 to 93.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PASI90 Response Rates by Visit

End point title	PASI90 Response Rates by Visit

End point description:

Percentage of PASI90 responders, defined as a 90% improvement in PASI score compared to baseline in subjects with ≥ 3% BSA psoriasis involvement at baseline. PASI assesses four anatomic sites (head, upper extremities, trunk, and lower extremities) for erythema, induration and desquamation related to psoriasis. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest possible degree. Typically, scores of 3 or less represent mild disease, scores over 3 and up and including 15 represent moderate disease, and scores over 15 are considered to be associated with severe disease. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=93	62.4 (52.2 to 71.5)			
Week 8; n=86	66.3 (55.8 to 75.4)			
Week 16; n=64	60.9 (48.7 to 72)			
Week 24; n=23	69.6 (48.9 to 84.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Disease Activity (MDA) in PsA Response Rate by Visit in Subjects with PASI > 3 at Baseline

End point title	Minimal Disease Activity (MDA) in PsA Response Rate by Visit in Subjects with PASI > 3 at Baseline

End point description:

A subject was classified as in MDA when 5 of the following 7 criteria are met: Tender Joint Count 68 ≤ 1; Swollen Joint Count 66 ≤ 1; PASI ≤ 1 or BSA ≤ 3; Patient Assessment of Pain ≤ 15; Patient Global Assessment ≤ 20; Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S) ≤ 0.5; tender entheseal points ≤ 1. Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Secondary

End point timeframe:

Week 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4; n=112	32.1 (24.2 to 41.3)			
Week 8; n=105	30.5 (22.5 to 39.9)			
Week 16; n=76	32.9 (23.3 to 44.1)			
Week 24; n=28	42.9 (26.5 to 60.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's Global Assessment for Psoriasis Score of 0 or 1 Response Rate by Visit

End point title	Physician's Global Assessment for Psoriasis Score of 0 or 1 Response Rate by Visit

End point description:

The physician assessed the severity of a subject's disease activity at the time of visit using a Physician's Global Assessment of Psoriasis 7-point scale. The scale ranges from 0 to 6. A higher score indicates more severe psoriasis activity, with 0 corresponding to "clear" and 6 corresponding to "severe." Estimates of the 95% confidence interval of the response rates for each treatment group were calculated using the Agresti-Coull method.

Safety Analysis Set: subjects who received ≥ 1 dose of study drug in Study M14-198; n=subjects who had an assessment at the given time point.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: percentage of participants				
number (confidence interval 95%)				
Week 4; n=164	75.6 (68.5 to 81.6)			
Week 8; n=157	79.6 (72.6 to 85.2)			
Week 16; n=118	79.7 (71.5 to 86)			

Week 24; n=45	88.9 (76 to 95.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriasis Target Lesion Score by Visit

End point title	Change From Baseline in Psoriasis Target Lesion Score by Visit

End point description:

Target lesion score for psoriasis in subjects with psoriatic arthritis is calculated by adding the scores of plaque erythema, scaling and thickness. Scores range from 0 (no erythema or evidence of plaque scaling and thickness) to 15 (severe erythema and evidence of plaque scaling and thickness).

Safety Analysis Set: all subjects who received ≥ 1 dose of study medication in Study M14-198; n=subjects available at both the specific visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=165	-4.95 (± 2.735)			
Week 8; n=158	-5.02 (± 2.665)			
Week 16; n=119	-4.98 (± 2.98)			
Week 24; n=45	-4.51 (± 2.582)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician's Global Assessment for Psoriasis by Visit

End point title	Change From Baseline in Physician's Global Assessment for Psoriasis by Visit

End point description:

The physician assessed the severity of a subject's disease activity at the time of visit using a Physician's Global Assessment of Psoriasis 7-point scale. The scale ranges from 0 to 6. A higher score indicates more severe psoriasis activity, with 0 corresponding to "clear" and 6 corresponding to "severe."

Safety Analysis Set: all subjects who received ≥ 1 dose of study medication in Study M14-198; n=subjects available at both the specific visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=164	-2.12 (± 1.326)			
Week 8; n=157	-2.14 (± 1.337)			
Week 16; n=118	-2.15 (± 1.325)			
Week 24; n=45	-2.02 (± 1.138)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PASI by Visit

End point title	Change From Baseline in PASI by Visit

End point description:

PASI assesses four anatomic sites (head, upper extremities, trunk, and lower extremities) for erythema, induration and desquamation related to psoriasis. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest possible degree. Typically, scores of 3 or less represent mild disease, scores over 3 and up and including 15 represent moderate disease, and scores over 15 are considered to be associated with severe disease.

Safety Analysis Set: all subjects who received ≥ 1 dose of study medication in Study M14-198; n=subjects available at both the specific visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=165	-7.56 (± 9.658)			

Week 8; n=158	-7.08 (± 8.626)			
Week 16; n=119	-6.75 (± 7.981)			
Week 24; n=45	-5.54 (± 5.741)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dactylitis by Visit

End point title	Change From Baseline in Dactylitis by Visit

End point description:

The dactylitis count was calculated as the number of digits (hands and feet) with presence of dactylitis. The count ranges from 0 to 20, with higher scores indicating more severe dactylitis.

Safety Analysis Set: all subjects who received ≥ 1 dose of study medication in Study M14-198; n=subjects available at both the specific visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=165	-2.98 (± 4.744)			
Week 8; n=158	-3.28 (± 4.911)			
Week 16; n=119	-3.31 (± 4.905)			
Week 24; n=45	-4.02 (± 5.496)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis by Visit

End point title	Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis by Visit

End point description:

The SPARCC enthesitis index is an outcome measure for enthesitis in spondyloarthritis. Tenderness at each of 16 site is quantified on a dichotomous basis: 0 means non-tender and 1 means tender. The

SPARCC enthesitis index is calculated by taking the sum of the scores from the 16 sites. The SPARCC score ranges from 0 to 16, with higher scores indicating more tenderness.

Safety Analysis Set: all subjects who received ≥ 1 dose of study medication in Study M14-198; n=subjects available at both the specific visit and baseline visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 16, 24

End point values	ABT-122			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4; n=165	-2.87 (± 3.563)			
Week 8; n=158	-2.99 (± 3.329)			
Week 16; n=119	-2.44 (± 4.163)			
Week 24; n=45	-2.89 (± 2.83)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Protocol-related treatment-emergent adverse events and treatment-emergent serious adverse events were collected from the first dose of study drug in study M14-198 until 70 days after the last dose of study drug (up to 32 weeks).

Adverse event reporting additional description:

A protocol-related event is defined as any AE with onset or worsening reported by a subject from the first dose of study drug in study M14-198 until 70 days have elapsed following discontinuation of ABT-122 administration. Events were collected whether elicited or spontaneously reported by the subject.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	ABT-122

Reporting group description:

Open-label ABT-122 240 mg EOW for 24 weeks

Serious adverse events	ABT-122		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 168 (0.60%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	1 / 168 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 168 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MUSCLE STRAIN			
subjects affected / exposed	1 / 168 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ROAD TRAFFIC ACCIDENT			

subjects affected / exposed	1 / 168 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	ABT-122		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 168 (47.02%)		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	9 / 168 (5.36%)		
occurrences (all)	11		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	5 / 168 (2.98%)		
occurrences (all)	7		
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	4		
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	3		
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	3		
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
CRYSTAL URINE PRESENT			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	5		
MONOCYTE COUNT INCREASED			

subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	3		
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	5 / 168 (2.98%)		
occurrences (all)	6		
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	9 / 168 (5.36%)		
occurrences (all)	9		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	3		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
DIARRHOEA			
subjects affected / exposed	4 / 168 (2.38%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
RHINORRHOEA			
subjects affected / exposed	3 / 168 (1.79%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
PSORIASIS			
subjects affected / exposed	7 / 168 (4.17%)		
occurrences (all)	9		
RASH			
subjects affected / exposed	4 / 168 (2.38%)		
occurrences (all)	4		
Renal and urinary disorders			

CRYSTALLURIA subjects affected / exposed occurrences (all)	4 / 168 (2.38%) 4		
GLYCOSURIA subjects affected / exposed occurrences (all)	2 / 168 (1.19%) 2		
PROTEINURIA subjects affected / exposed occurrences (all)	3 / 168 (1.79%) 3		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	6 / 168 (3.57%) 7		
BACK PAIN subjects affected / exposed occurrences (all)	3 / 168 (1.79%) 3		
INTERVERTEBRAL DISC DISORDER subjects affected / exposed occurrences (all)	2 / 168 (1.19%) 2		
PSORIATIC ARTHROPATHY subjects affected / exposed occurrences (all)	7 / 168 (4.17%) 8		
TENDON DISORDER subjects affected / exposed occurrences (all)	2 / 168 (1.19%) 2		
Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all)	2 / 168 (1.19%) 2		
INFLUENZA subjects affected / exposed occurrences (all)	3 / 168 (1.79%) 3		
NASOPHARYNGITIS subjects affected / exposed occurrences (all)	6 / 168 (3.57%) 6		
ORAL HERPES			

subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
PHARYNGITIS			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
RHINITIS			
subjects affected / exposed	4 / 168 (2.38%)		
occurrences (all)	4		
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	3		
TONSILLITIS			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 168 (5.95%)		
occurrences (all)	11		
URINARY TRACT INFECTION			
subjects affected / exposed	5 / 168 (2.98%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	9 / 168 (5.36%)		
occurrences (all)	9		
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	4 / 168 (2.38%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2015	The purpose of this amendment was to: ● Extend enrollment to a maximum of 220 subjects to allow all eligible subjects to have the option to participate. ● Increase the number of participating sites for consistency with the number of sites in the RCT. ● Revise wording for the approved birth control methods to ensure that only highly effective contraceptive measures were allowed, consistent with the recommendations related to contraception and pregnancy testing in clinical trials by the European Union Clinical Trial Facilitation Group (Heads of Medicines Agencies). ● Clarify the visits that had a 3-day visit window. ● Add electrocardiogram (ECG) at Week 0 and optional ECG at Week 24 to study procedures. ● Add assessment instructions in the event of an injection site reaction. ● Correct test names and clarification of microscopic urinalysis testing. ● Update study procedures to include Patient Global Disease Activity for Arthritis visual analog scale Patient's Global Assessment of Disease Activity (PtGA) assessments at the Week 4, 8, 16, 24/Premature Discontinuation visits. ● Remove 24 hour Methylhistamine assay deleted from hypersensitivity reaction panel. ● Add criteria for extra dose eligibility. ● Update of primary study contact. ● Add detail to comparison point for ACR 20/50/70 response assessment. ● Add details regarding the use of ePro devices for data collection. ● Apply administrative changes throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported