Clinical trial results:
A Phase 4 Open-label Randomized Controlled Study COmparing the Effectiveness of Adalimumab iNTROduction and Methotrexate Dose escaLation in Subjects With Psoriatic Arthritis (CONTROL)

Summary

EudraCT number	2016-000191-21
Trial protocol	BG GB PL CZ ES DE IT
Global end of trial date	19 March 2020

Results information

Result version number	v1 (current)
This version publication date	23 December 2020
First version publication date	23 December 2020

Trial information

Trial identification

Sponsor protocol code	M14-496

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02814175
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@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	19 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

An interventional Phase 4 open-label, randomized, controlled, parallel-group, multi-country study in participants with psoriatic arthritis (PsA) consisting of 2 parts: Part 1 is designed to compare the achievement of minimal disease activity (MDA) between participants randomized to either adalimumab in combination with methotrexate (MTX) or MTX alone escalated to the highest recommended or tolerable dose; Part 2 is designed to evaluate the maintenance or achievement of MDA on 4 different treatment regimens using adalimumab and/or MTX, with participant allocation based on the initial randomized treatment and achievement of MDA in Part 1, and with rescue treatment option.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator:

MTX is the most commonly prescribed csDMARD in PsA, but its recommended dosing has been extrapolated from clinical trials in RA.

Actual start date of recruitment	05 August 2016
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	Australia: 20
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Bulgaria: 45
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Puerto Rico: 25
Country: Number of subjects enrolled	Qatar: 3
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	245
EEA total number of subjects	122

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)	209
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Intent-To-Treat Part 1 (ITT Part 1) population comprised all participants who were randomized and received at least 1 dose of study drug. 246 participants were randomized; 1 participant did not receive study drug. Upon completion of Part 1, eligible participants continued to Part 2, so no additional participants were enrolled in Part 2.

Pre-assignment

Screening details:

The Intent-To-Treat Part 1 (ITT Part 1) population comprised all participants who were randomized and received at least 1 dose of study drug and is the population for baseline characteristics. The ITT Long Term (ITT LT) population included all participants who entered Part 2 from Part 1 and received at least 1 dose of Part 2 study drug.

Period 1

Period 1 title	Part 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: MTX Escalated Dose

Arm description:

Methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew)

Arm type	Active comparator
Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Tablet
Routes of administration	Subcutaneous use, Oral use

Dosage and administration details:

MTX escalated to 20 -25 mg or highest tolerable dose ew

Arm title	Part 1: ADA + MTX

Arm description:

Adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 15 mg ew

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab (ADA) 40 mg every other week (eow) in combination with methotrexate (MTX) 15 mg every week (ew)

Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Injection
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

Adalimumab (ADA) 40 mg every other week (eow) in combination with methotrexate (MTX) 15 mg

every week (ew)

Number of subjects in period 1	Part 1: MTX Escalated Dose	Part 1: ADA + MTX
Started	122	123
Completed	110	117
Not completed	12	6
Adverse event, non-fatal	2	3
Lost to follow-up	1	-
Withdrawal Consent	8	1
Lack of efficacy	1	2

Period 2	
Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 2: MTX Escalated Dose

Arm description:

Participants achieving minimal disease activity (MDA) at Week 16 on MTX escalated to 20 -25 mg or highest tolerable dose ew, continued with the same MTX dose

Arm type	Active comparator
Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Tablet
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

MTX escalated to 20 -25 mg or highest tolerable dose ew

Arm title	Part 2: ADA + MTX Escalated Dose

Arm description:

Participants not achieving minimal disease activity (MDA) at Week 16 on methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable
dose every week (ew), received adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 20 - 25 mg or highest tolerable dose ew

Arm type	Active comparator

Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Tablet
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

MTX escalated to 20 -25 mg or highest tolerable dose ew

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab (ADA) 40 mg every other week (eow) in combination with methotrexate (MTX) 20 - 25 mg or highest tolerable dose ew

Arm title	Part 2: ADA

Arm description:

Participants achieving minimal disease activity (MDA) at Week 16 on adalimumab (ADA) 40 mg every other week (eow) plus methotrexate (MTX) 15 mg every week (ew), had MTX completely withdrawn at Week 16 and continued receiving ADA as monotherapy

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab (ADA) 40 mg every other week (eow)

Arm title	Part 2: ADA ew + MTX

Arm description:

Participants not achieving minimal disease activity (MDA) at Week 16 on ADA 40 mg every other week (eow) plus methotrexate (MTX) 15 mg every week (ew), had ADA escalated to 40 mg ew in combination with MTX 15 mg ew

Arm type	Experimental
Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Tablet
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

MTX dosed at 15 mg ew

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab (ADA) escalated to 40 mg every week (ew) in combination with methotrexate (MTX) 15 mg every week (ew)

Number of subjects in period 2	Part 2: MTX Escalated Dose	Part 2: ADA + MTX Escalated Dose	Part 2: ADA
Started	15	95	54
Completed	15	91	52
Not completed	0	4	2
Adverse event, non-fatal	-	1	1
Lost to follow-up	-	1	-
Withdrawal Consent	-	2	1
Lack of efficacy	-	-	-

Number of subjects in period 2	Part 2: ADA ew + MTX
Started	63
Completed	57
Not completed	6
Adverse event, non-fatal	2
Lost to follow-up	-
Withdrawal Consent	1
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: MTX Escalated Dose
Reporting group description:	
Methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew)	
Reporting group title	Part 1: ADA + MTX
Reporting group description:	
Adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 15 mg ew	

Reporting group values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX	Total
Number of subjects	122	123	245
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	48.8	51.4	
standard deviation	± 12.69	± 12.23	-
Gender categorical Units: Subjects			
Female	59	64	123
Male	63	59	122

Subject analysis sets	
Subject analysis set title	ITT Part 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-treat (ITT Part 1) population comprises all participants who were randomized and received at least one dose of the study medication.	

Reporting group values	ITT Part 1		
Number of subjects	245		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	50.1		
standard deviation	± 12.50		
Gender categorical Units: Subjects			
Female	123		
Male	122		

End points

End points reporting groups

Reporting group title	Part 1: MTX Escalated Dose
Reporting group description:	
Methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew)	
Reporting group title	Part 1: ADA + MTX
Reporting group description:	
Adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 15 mg ew	
Reporting group title	Part 2: MTX Escalated Dose
Reporting group description:	
Participants achieving minimal disease activity (MDA) at Week 16 on MTX escalated to 20 -25 mg or highest tolerable dose ew, continued with the same MTX dose	
Reporting group title	Part 2: ADA + MTX Escalated Dose
Reporting group description:	
Participants not achieving minimal disease activity (MDA) at Week 16 on methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew), received adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 20 - 25 mg or highest tolerable dose ew	
Reporting group title	Part 2: ADA
Reporting group description:	
Participants achieving minimal disease activity (MDA) at Week 16 on adalimumab (ADA) 40 mg every other week (eow) plus methotrexate (MTX) 15 mg every week (ew), had MTX completely withdrawn at Week 16 and continued receiving ADA as monotherapy	
Reporting group title	Part 2: ADA ew + MTX
Reporting group description:	
Participants not achieving minimal disease activity (MDA) at Week 16 on ADA 40 mg every other week (eow) plus methotrexate (MTX) 15 mg every week (ew), had ADA escalated to 40 mg ew in combination with MTX 15 mg ew	
Subject analysis set title	ITT Part 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-treat (ITT Part 1) population comprises all participants who were randomized and received at least one dose of the study medication.	

Primary: Percentage of Participants Achieving Minimal Disease Activity (MDA) (Non-responder Imputation [NRI]) (Part 1)

End point title	Percentage of Participants Achieving Minimal Disease Activity (MDA) (Non-responder Imputation [NRI]) (Part 1)
End point description:	
Minimal disease activity (MDA) for psoriatic arthritis (PsA) was defined as fulfilling at least 5 of the following 7 criteria: tender and swollen joint counts (TJC) ≤ 1 (out of TJC68 assessed in this study), swollen joint count (SJC) ≤ 1 (out of SJC66 assessed in this study), Psoriasis Area and Severity Index (PASI) ≤ 1 or body surface area (BSA) ≤ 3; Patient's assessment of pain visual analogue scale (VAS) ≤ 15, Patient's global assessment of disease activity (PtGA) VAS ≤ 20, Health Assessment Questionnaire Disability Index (HAQ-DI) score ≤ 0.5, and tender entheseal points ≤ 1 (out of 8 assessed in this study). Analysis population: Intent-To-Treat Part 1 (ITT Part 1) population comprises all participants who were randomized and received at least one dose of the study medication during Part 1. Results for binary endpoints are based on non-responder imputation (NRI).	
End point type	Primary
End point timeframe:	
Week 16	

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	123		
Units: percentage of participants				
arithmetic mean (confidence interval 95%)	13.1 (7.1 to 19.1)	41.5 (32.8 to 50.2)		

Statistical analyses

Statistical analysis title	Between Group Difference
Comparison groups	Part 1: MTX Escalated Dose v Part 1: ADA + MTX
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	point estimate difference
Point estimate	28.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.8
upper limit	38.9

Notes:

[1] - Between group difference

Secondary: Change in Dermatology Life Quality Index (DLQI) Score From Baseline (Part 1)

End point title	Change in Dermatology Life Quality Index (DLQI) Score From Baseline (Part 1)

End point description:

The Dermatology Life Quality Index (DLQI) score is a measure of participant's quality of life (QOL) related to skin disease. The DLQI questionnaire consists of 10 questions concerning participants' perception of the impact of skin diseases on different aspects of their health related QOL over the last week. The items of the DLQI encompass aspects such as symptoms and feelings, daily activities, leisure, work or school, personal relationships and the side effects of treatment. The range of possible DLQI scores was 0 to 30, with a score of 0 indicating no effect at all on a participant's life and a score of 30 indicating extremely large effect on participant's life. A decrease in DLQI score indicates improvement. Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	117		
Units: point estimate				
least squares mean (confidence interval 95%)	-3.1 (-3.85 to -2.30)	-5.9 (-6.70 to -5.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Tender Dactylitic Digit Count From Baseline for Participants With Presence of Dactylitis at Baseline (Part 1)

End point title	Change in Tender Dactylitic Digit Count From Baseline for Participants With Presence of Dactylitis at Baseline (Part 1)

End point description:

Hands and feet bilaterally were assessed for the presence/absence of dactylitis and associated tenderness for participants with the presence of dactylitis at baseline. The tender dactylitic digit count is equal to the number of swollen and painful digits (range 0 to 20). A decrease indicates improvement.

Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	62		
Units: count of fingers/ toes with dactylitis				
least squares mean (confidence interval 95%)	-0.9 (-1.48 to -0.41)	-2.8 (-3.35 to -2.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score 28 (DAS28)-C-reactive Protein (CRP) Score From Baseline (Part 1)

End point title	Change in Disease Activity Score 28 (DAS28)-C-reactive Protein (CRP) Score From Baseline (Part 1)

End point description:

The Disease Activity Score 28 (DAS28) is a validated index of rheumatoid arthritis disease activity but is also used in PsA clinical trials. DAS28 is a composite score calculated using a mathematical formula based on the scores for these scales. DAS28 includes tender and swollen joint counts, PtGA, and acute phase reactant (CRP in this study). DAS28 scores range from 0 to 10, with higher scores indicating more

disease activity. A larger negative change in the DAS28 score indicates greater improvement.

Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	114		
Units: scores on a scale				
least squares mean (confidence interval 95%)	-0.9 (-1.08 to -0.65)	-2.0 (-2.16 to -1.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Psoriatic Arthritis Impact of Disease Score (PsAID) Score From Baseline (Part 1)

End point title	Change in Psoriatic Arthritis Impact of Disease Score (PsAID) Score From Baseline (Part 1)

End point description:

Psoriatic Arthritis Impact of Disease Score (PsAID) was developed by an European League Against Rheumatism (EULAR) initiative and is a validated patient self-reported tool to assess the impact of PsA on the participant's life. The PsAID is a composite score calculated using a mathematical formula based on the scores for each component. PsAID-9 was developed for clinical trials and was used in this study. The PsAID-9 is calculated based on 9 Numerical rating scales (NRS) questions that include pain, fatigue, skin, work and/or leisure activities, function, discomfort, sleep, coping, and anxiety). Each NRS is assessed as a number between 0 and 10. PsAID scores range from 0 to 10, with higher scores indicating worse status. A larger negative change in the PsAID-9 score indicates greater improvement.

Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	117		
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.7 (-2.09 to -1.28)	-3.3 (-3.73 to -2.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology (ACR) 20/50/70 Response (Part 1)

End point title	Percentage of Participants Achieving American College of Rheumatology (ACR) 20/50/70 Response (Part 1)

End point description:

The ACR is a standard criteria originally developed to measure the effectiveness of various arthritis medications or treatments in clinical trials for RA, but is also widely used in PsA. The ACR measures improvement in tender joint count (TJC) or swollen joint count (SJC), and improvement in at least 3 of the following 5 parameters: Patient Global Assessment (PtGA), Physician's Global Assessment of Disease Activity (PhGA), physical function (using HAQ-DI) and acute phase reactant (using CRP). ACR 20/50/70 response is achieved if ≥ 20%/≥ 50%/≥ 70% improvement in tender joint count (TJC) or swollen joint count (SJC) as well as a ≥ 20%/≥ 50%/≥ 70% improvement in ≥ 3 of the other 5 parameters.

Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	123		
Units: percentage of participants				
arithmetic mean (confidence interval 95%)				
ACR 20	32.8 (24.5 to 41.1)	67.5 (59.2 to 75.8)		
ACR 50	16.4 (9.8 to 23.0)	45.5 (36.7 to 54.3)		
ACR 70	8.2 (3.3 to 13.1)	30.9 (22.7 to 39.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Leeds Enthesitis Index (LEI) From Baseline (Part 1) for Participants With Presence of LEI at Baseline

End point title	Change in Leeds Enthesitis Index (LEI) From Baseline (Part 1) for Participants With Presence of LEI at Baseline

End point description:

The Leeds Enthesitis Index (LEI) is an enthesitis measure developed specifically for PsA and assesses the presence or absence of tenderness at the following 3 bilateral enthesial sites: medial femoral condyles, lateral epicondyles of the humerus, and Achilles tendon insertions for participants with presence of LEI at baseline. Tenderness on examination is recorded as either present (1) or absent (0) for each of the 6 sites, for an overall score range of 0 to 6. A decrease in LEI indicates improvement.

Analysis population: ITT (Part 1). Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	92		
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.1 (-1.43 to -0.75)	-1.9 (-2.22 to -1.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in MDA in Part 2 of the Study (Week 32)

End point title	Percentage of Participants in MDA in Part 2 of the Study (Week 32)

End point description:

MDA for PsA was defined as fulfilling at least 5 of the following 7 criteria: TJC ≤ 1 (out of TJC68 assessed in this study), SJC ≤ 1 (out of SJC66 assessed in this study), PASI ≤ 1 or BSA ≤ 3; Patient's assessment of pain VAS ≤ 15, PtGA VAS ≤ 20, HAQ-DI score ≤ 0.5, and tender entheseal points ≤ 1 (out of 8 assessed in this study).

Analysis population: ITT Long Term (ITT LT) population comprises all participants who continued to Part 2 and received at least one dose of Part 2 study medication. No missing data imputation performed for long term efficacy analysis except for participants who were rescued, where participants rescued prior to Week 32 are imputed as non-responders.

End point type	Secondary

End point timeframe:

Week 32

End point values	Part 2: MTX Escalated Dose	Part 2: ADA + MTX Escalated Dose	Part 2: ADA	Part 2: ADA ew + MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	91	51	57
Units: percentage of participants				
arithmetic mean (confidence interval	66.7 (42.8 to	54.9 (44.7 to	80.4 (69.5 to	29.8 (17.9 to

95%)	90.5)	65.2)	91.3)	41.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Psoriatic Arthritis Disease Activity Score (PASDAS) From Baseline (Part 1)

End point title	Change in Psoriatic Arthritis Disease Activity Score (PASDAS) From Baseline (Part 1)

End point description:

Psoriatic Arthritis Disease Activity Score (PASDAS) is a weighted disease activity measure developed specifically for PsA. It includes PhGA, PtGA, SF-36 PCS, SJC, TJC, Leeds enthesitis count, tender dactylitic count and hsCRP lab test. The PASDAS is a composite score calculated using a mathematical formula based on the scores for each component. The PASDAS is unitless, with a typical score range between 0 and 10. Smaller values on PASDAS indicate a better condition; a negative change from baseline indicates improvement.

Analysis population: ITT (Part 1) Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	114		
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.2 (-1.46 to -0.86)	-2.8 (-3.05 to -2.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form Health Survey 36 (SF-36) Score From Baseline (Part 1)

End point title	Change in Short Form Health Survey 36 (SF-36) Score From Baseline (Part 1)

End point description:

The Short Form Health Survey 36 (SF-36) is a generic measure to assess participant's general health/well-being (health related quality of life); short version 2 was used. SF-36 determined participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items

1-4 are the physical component. Scores on each item were summed and averaged (PCS; range = 0-100). Items 5-8 are the mental component. Scores on each item were summed and averaged (mental component score [MCS]; range = 0-100). Larger values indicate a better condition. A positive change from Baseline in either PCS or MCS indicates improvement. Analysis population: ITT Part 1.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	117		
Units: score on a scale				
least squares mean (confidence interval 95%)				
SF-36 PCS	4.4 (3.07 to 5.73)	8.9 (7.58 to 10.15)		
SF-36 MCS	1.3 (-0.36 to 2.97)	4.4 (2.85 to 6.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HAQ-DI Score From Baseline (Part 1)

End point title	Change in HAQ-DI Score From Baseline (Part 1)

End point description:

The HAQ-DI is a standardized measure of physical function in arthritis. The HAQ-DI questionnaire contains 20 items divided into 8 domains that measure: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task were summed and averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 very severe, high-dependency disability. HAQ remission indicating normal physical function is defined by HAQ-DI score of < 0.5. Negative change from Baseline indicates improvement.
Analysis population: ITT (Part 1) Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	116		
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.3 (-0.39 to -0.21)	-0.5 (-0.60 to -0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Psoriasis Area and Severity Index (PASI) 75/90/100 Response Among Participants With BSA Greater Than or Equal to 3% at Baseline (Part 1)

End point title	Percentage of Participants Achieving Psoriasis Area and Severity Index (PASI) 75/90/100 Response Among Participants With BSA Greater Than or Equal to 3% at Baseline (Part 1)

End point description:

Psoriasis Area and Severity Index (PASI) provides a quantitative assessment of psoriasis lesional burden based on the amount of body surface area involved and the degree of severity of erythema, induration, and scale, weighted by body part. The score ranges from 0 to 72, with 0 indicating no psoriasis and 72 indicating very severe psoriasis. 75/90/100 denotes greater than or equal to 75%/90%/100% improvement in PASI score. A 100% reduction is considered complete clearance of psoriasis.

Analysis population: ITT (Part 1) Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	78		
Units: percentage of participants				
arithmetic mean (confidence interval 95%)				
PASI 75	31.0 (21.3 to 40.8)	73.1 (63.2 to 82.9)		
PASI 90	18.4 (10.3 to 26.5)	57.7 (46.7 to 68.7)		
PASI 100	9.2 (3.1 to 15.3)	29.5 (19.4 to 39.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity in Psoriatic Arthritis Score (DAPSA) Score From Baseline (Part 1)

End point title	Change in Disease Activity in Psoriatic Arthritis Score (DAPSA) Score From Baseline (Part 1)

End point description:

Disease Activity in Psoriatic Arthritis Score (DAPSA) score is a the sum of swollen joint count (66 joints), tender joint count (68 joints), CRP (mg/dL), Patient's Assessment of Pain (on a 10-unit VAS;0=no pain, 10=worst possible pain), and Patient's Global Assessment of Disease Activity (arthritis, on a 10-unit VAS; 0 to 100 centimeter [cm] VAS, 0=excellent and 10=poor). Change from baseline in DAPSA measures the change in disease activity, where a negative change indicates an improvement and a positive change indicates worsening of disease activity.

Analysis population: ITT (Part 1) Results for binary endpoints are based on NRI. Results for other continuous endpoints are based on MMRM.

End point type	Secondary

End point timeframe:

From Day 1 to Week 16

End point values	Part 1: MTX Escalated Dose	Part 1: ADA + MTX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	114		
Units: score on a scale				
least squares mean (confidence interval 95%)	-12.1 (-15.57 to -8.69)	-28.2 (-31.60 to -24.87)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported from the time of study drug administration until 70 days following discontinuation of study drug administration have elapsed

Adverse event reporting additional description:

Two sets safety analyses performed: Safety Population Part 1 (received at least 1 dose Part 1 study medication [1 of 2 treatment arms]) analyses during Part 1 (up to Week 16) and Safety Population Part 2 (received at least 1 dose of Part 2 study medication [1 of 4 treatment arms]) analyses during Part 2 (Week 16 to Week 32).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Part 1: MTX Escalated

Reporting group description:

Methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew) (MTX 20 - 25 mg or highest tolerable dose ew)

Reporting group title	Part 1: ADA + MTX

Reporting group description:

Adalimumab (ADA) 40 mg every other week (eow) in combination with MTX 15 mg ew (ADA 40 mg eow + MTX 15 mg ew

Reporting group title	Part 2: ADA

Reporting group description:

Participants achieving MDA at Week 16 on ADA 40 mg eow plus MTX 15 mg ew, had MTX completely withdrawn at Week 16 and continued receiving ADA as monotherapy (ADA 40 mg eow)

Reporting group title	Part 2: ADA ew +MTX

Reporting group description:

Participants not achieving MDA at Week 16 on ADA 40 mg eow plus MTX 15 mg ew, had ADA escalated to 40 mg ew in combination with MTX 15 mg ew (ADA 40 mg ew plus MTX 15 mg ew)

Reporting group title	Part 2: MTX Escalated Dose

Reporting group description:

Participants achieving MDA at Week 16 on MTX escalated to 20 -25 mg or highest tolerable dose ew, continued with the same MTX dose (MTX 20 - 25 mg or highest tolerable dose ew)

Reporting group title	Part 2: ADA +MTX Escalated Dose

Reporting group description:

Participants not achieving MDA at Week 16 on MTX escalated to 20 - 25 mg or highest tolerable dose ew, received ADA 40 mg eow in combination with MTX 20 - 25 mg or highest tolerable dose ew (ADA 40 mg eow plus MTX 20 - 25 mg or highest tolerable dose ew)

Serious adverse events	Part 1: MTX Escalated	Part 1: ADA + MTX	Part 2: ADA
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 122 (0.00%)	2 / 123 (1.63%)	1 / 54 (1.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			

ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
SCIATICA			
subjects affected / exposed	0 / 122 (0.00%)	1 / 123 (0.81%)	0 / 54 (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
Gastrointestinal disorders			
GASTRIC MUCOSA ERYTHEMA			

subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
GASTRITIS			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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			
UTERINE POLYP			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
DIVERTICULITIS			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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
PNEUMONIA			
subjects affected / exposed	0 / 122 (0.00%)	1 / 123 (0.81%)	0 / 54 (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
SUBCUTANEOUS ABSCESS			

subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (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

Serious adverse events	Part 2: ADA ew +MTX	Part 2: MTX Escalated Dose	Part 2: ADA +MTX Escalated Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 63 (4.76%)	0 / 15 (0.00%)	3 / 95 (3.16%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 63 (1.59%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR VERTEBRAL FRACTURE			

subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	0 / 95 (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
Nervous system disorders			
SCIATICA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	0 / 95 (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
Gastrointestinal disorders			
GASTRIC MUCOSA ERYTHEMA			
subjects affected / exposed	1 / 63 (1.59%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	1 / 63 (1.59%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
UTERINE POLYP			
subjects affected / exposed	1 / 63 (1.59%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 63 (1.59%)	0 / 15 (0.00%)	0 / 95 (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
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
DIVERTICULITIS			

subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	0 / 95 (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
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part 1: MTX Escalated	Part 1: ADA + MTX	Part 2: ADA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 122 (32.79%)	35 / 123 (28.46%)	3 / 54 (5.56%)
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 122 (4.92%)	5 / 123 (4.07%)	1 / 54 (1.85%)
occurrences (all)	7	5	2
TRANSAMINASES INCREASED			
subjects affected / exposed	2 / 122 (1.64%)	1 / 123 (0.81%)	0 / 54 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	2 / 122 (1.64%)	10 / 123 (8.13%)	0 / 54 (0.00%)
occurrences (all)	3	10	0
General disorders and administration site conditions			
DRUG INTOLERANCE			
subjects affected / exposed	8 / 122 (6.56%)	0 / 123 (0.00%)	0 / 54 (0.00%)
occurrences (all)	12	0	0
Gastrointestinal disorders			

NAUSEA			
subjects affected / exposed	11 / 122 (9.02%)	5 / 123 (4.07%)	0 / 54 (0.00%)
occurrences (all)	13	5	0
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	1 / 122 (0.82%)	7 / 123 (5.69%)	0 / 54 (0.00%)
occurrences (all)	1	8	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	4 / 122 (3.28%)	3 / 123 (2.44%)	1 / 54 (1.85%)
occurrences (all)	4	3	1
PSORIATIC ARTHROPATHY			
subjects affected / exposed	3 / 122 (2.46%)	3 / 123 (2.44%)	0 / 54 (0.00%)
occurrences (all)	3	3	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	2 / 122 (1.64%)	2 / 123 (1.63%)	0 / 54 (0.00%)
occurrences (all)	2	2	0
NASOPHARYNGITIS			
subjects affected / exposed	3 / 122 (2.46%)	5 / 123 (4.07%)	1 / 54 (1.85%)
occurrences (all)	3	5	1
PNEUMONIA			
subjects affected / exposed	0 / 122 (0.00%)	0 / 123 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	11 / 122 (9.02%)	10 / 123 (8.13%)	2 / 54 (3.70%)
occurrences (all)	11	10	2

Non-serious adverse events	Part 2: ADA ew +MTX	Part 2: MTX Escalated Dose	Part 2: ADA +MTX Escalated Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 63 (17.46%)	5 / 15 (33.33%)	17 / 95 (17.89%)

Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 63 (4.76%)	1 / 15 (6.67%)	2 / 95 (2.11%)
occurrences (all)	5	1	4
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 63 (1.59%)	1 / 15 (6.67%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
DRUG INTOLERANCE			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	0 / 95 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	1 / 63 (1.59%)	1 / 15 (6.67%)	4 / 95 (4.21%)
occurrences (all)	1	1	4
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 63 (0.00%)	1 / 15 (6.67%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 63 (0.00%)	0 / 15 (0.00%)	2 / 95 (2.11%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	4 / 63 (6.35%)	0 / 15 (0.00%)	1 / 95 (1.05%)
occurrences (all)	4	0	1
PSORIATIC ARTHROPATHY			
subjects affected / exposed	4 / 63 (6.35%)	1 / 15 (6.67%)	0 / 95 (0.00%)
occurrences (all)	4	1	0
Infections and infestations			

BRONCHITIS			
subjects affected / exposed	0 / 63 (0.00%)	1 / 15 (6.67%)	1 / 95 (1.05%)
occurrences (all)	0	1	1
NASOPHARYNGITIS			
subjects affected / exposed	2 / 63 (3.17%)	0 / 15 (0.00%)	6 / 95 (6.32%)
occurrences (all)	2	0	6
PNEUMONIA			
subjects affected / exposed	1 / 63 (1.59%)	1 / 15 (6.67%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	9 / 63 (14.29%)	0 / 15 (0.00%)	13 / 95 (13.68%)
occurrences (all)	11	0	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2016	Major changes included: included all known potential risks associated with adalimumab; allowed for the inclusion of subjects that may have short-term MTX dose decrease or withdrawal for various reasons during the required prior MTX 15 mg ew course of up to 36-week duration; applied a stricter inclusion criterion to increase safety of subjects taking MTX; extended the screening window in certain circumstances; updated rescreening procedures for clarity; updated the contraception recommendation; included HIV testing for subjects that may be at risk for HIV infection; removed scanning for the presence of erosions as methodologically not sufficiently standardized in PsA; revised TB screening procedures; specified subjects that develop TB or any other serious or opportunistic infection must discontinue study treatment and ensure appropriate subject discontinuation in alignment with risks associated with study drug; clarified the reference document used for SUSAR reporting in the EU countries for adalimumab will be the most current version of SmPC; specified that substantial amendments must be reviewed and approved by the competent authority.
09 March 2018	Updated safety information to refer to SmPC or prescribing information; updated inclusion criteria to: remove upper limit of 36 weeks for prior MTX 15 mg ew use; updated inclusion criteria to change the timepoint from Screening to Baseline as Baseline is the standard time point prior to and for certain time periods stable doses of oral corticosteroids and csDMARDS are required; change required stability period of oral corticosteroids to 1 week prior to Baseline; change the required stability period of NSAID and paracetamol dosing to 1 week prior to Baseline and clarify dose of paracetamol; require 4 week washout of leflunomide prior to Baseline and prohibited medication to include leflunomide; updated exclusion criteria to: change time point from Screening to Baseline as Baseline is the standard to evaluate whether participant fulfilled appropriate time period of prohibited corticosteroids, joint surgeries, phototherapy, psoriasis therapy, vaccinations, drug or alcohol abuse, infections or anti-infectives, and joint infections for randomization into the study; allow history of fibromyalgia at Baseline while still excluding active fibromyalgia; added exclusion of apremilast and janus kinase inhibitors within 4 weeks of Baseline; added requirement for participants taking tramadol or equivalent opioids and/or non-opioid analgesics and narcotics in fixed combination with acetaminophen be at a stable dose for at least 1 week prior to Baseline; allowed use of NSAIDs and paracetamol at a stable dose during study from 1 week prior to baseline visit and, if used for a reason other than PsA, also on an as-needed basis if used for the same reason and same dose each time; allowed use of tramadol or equivalent opioids and/or non-opioid analgesics and narcotics in fixed combination with acetaminophen at a stable dose during study; prohibited joint surgeries during study; clarified CASPAR criteria to be assessed at Screening; added joint surgeries to reasons for discontinuation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported