Clinical trial results:
Multicenter, Open-Label Study to Assess the Effects of Certolizumab Pegol on the Reduction of Anterior Uveitis Flares in Axial Spondyloarthritis Subjects with a History of Anterior Uveitis (C-VIEW)

Summary

EudraCT number	2016-000343-14
Trial protocol	DE ES CZ NL
Global end of trial date	23 January 2020

Results information

Result version number	v1 (current)
This version publication date	05 February 2021
First version publication date	05 February 2021

Trial information

Trial identification

Sponsor protocol code	AS0007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03020992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SPRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, B-1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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	26 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the effect of Certolizumab Pegol (CZP) treatment on the reduction of Anterior Uveitis (AU) flares in subjects with active Axial Spondyloarthritis (axSpA) and a documented history of AU.

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not Applicable

Actual start date of recruitment	21 December 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	Czechia: 35
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 38
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	89
EEA total number of subjects	89

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)	84
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first participant was enrolled in December 2016 and the last participant was enrolled in December 2017.

Pre-assignment

Screening details:

The study included 3 periods as follows: Period 1 (Screening Period) 1 to 5 weeks before Baseline, Period 2 (Treatment Period) Week 0 to Week 96 and Period 3 (FU Period) 10 weeks from the final dose of investigational medicinal product (IMP) received (Week 104).
Participant Flow refers to the Safety Set.

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	Certolizumab Pegol

Arm description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 milligrams (mg) subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc every 2 weeks (Q2W) (starting at Week 6 until Week 94).

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

Dosage and administration details:

Certolizumab Pegol (CZP) 400 mg or 200 mg was administered as subcutaneous (sc) injections every 2 weeks.
Suitable areas for administrations were the lateral abdominal wall and upper outer thigh.

Number of subjects in period 1	Certolizumab Pegol
Started	89
Completed	83
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	5

Baseline characteristics

Reporting groups	
Reporting group title	Certolizumab Pegol
Reporting group description:	
Participants received a loading dose of Certolizumab Pegol (CZP) 400 milligrams (mg) subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc every 2 weeks (Q2W) (starting at Week 6 until Week 94).	

Reporting group values	Certolizumab Pegol	Total	
Number of subjects	89	89	
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	84	84	
>=65 years	5	5	
Age continuous Units: years			
arithmetic mean	46.52		
standard deviation	± 11.24	-	
Gender categorical Units: Subjects			
Female	33	33	
Male	56	56	

End points

End points reporting groups

Reporting group title	Certolizumab Pegol

Reporting group description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 milligrams (mg) subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc every 2 weeks (Q2W) (starting at Week 6 until Week 94).

Subject analysis set title	Certolizumab Pegol (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 mg subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc Q2W (starting at Week 6 until Week 94).

Subject analysis set title	Certolizumab Pegol (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 mg subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc Q2W (starting at Week 6 until Week 94).

Subject analysis set title	Certolizumab Pegol - Pre-study/Historical (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Pre-study was before IMP start and included 2 years (104 weeks) prior to Baseline.
This group is used in the primary efficacy analysis, to compare the frequency of AU flares during the pre-study/historical period with that observed while in the study during CZP treatment.

Subject analysis set title	Certolizumab Pegol - On-study (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 mg subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc Q2W (starting at Week 6 until Week 94).

Primary: Number of distinct episodes of Anterior Uveitis (AU) flares during the Treatment Period

End point title	Number of distinct episodes of Anterior Uveitis (AU) flares during the Treatment Period

End point description:

A flare was defined as being a new episode of Anterior Uveitis (AU) that, based on the judgment of an ophthalmologist, required specific treatment. A flare was considered a new episode if a gap of at least 3 months occurred between 2 flares.
The Full Analysis Set (FAS) consisted of all study participants in the Safety Set (SS) with nonmissing Baseline values for the primary efficacy variable (AU flare incidence data from the prestudy period).

End point type	Primary

End point timeframe:

During the pre-study period and during the Treatment Period up to 96 weeks

End point values	Certolizumab Pegol - Pre-study/Historical (FAS)	Certolizumab Pegol - On-study (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89	89		
Units: flares				
arithmetic mean (standard deviation)	1.9 (± 0.9)	0.3 (± 0.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The Poisson regression allowed for a comparison of event rates adjusting for differences in time between prestudy/on-study periods.
Event rates were based on a Poisson model with generalized estimating equations and a loglink, including an offset term for time interval length, and with period and disease duration of axSpA (<2 years/≥2 years) as covariates. A repeated statement was included for participants and assumed an exchangeable correlation structure between prestudy and on-study flares.

Comparison groups	Certolizumab Pegol - Pre-study/Historical (FAS) v Certolizumab Pegol - On-study (FAS)
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Poisson regression
Parameter estimate	Rate ratio
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.116
upper limit	0.281

Secondary: Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and a history of AU at Week 48

End point title	Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and a history of AU at Week 48

End point description:

A flare was defined as being a new episode of Anterior Uveitis (AU) that, based on the judgment of an ophthalmologist, required specific treatment. A flare was considered a new episode if a gap of at least 3 months occurred between 2 flares.
The Full Analysis Set (FAS) consisted of all study participants in the Safety Set (SS) with nonmissing Baseline values for the primary efficacy variable (AU flare incidence data from the prestudy period).

End point type	Secondary

End point timeframe:

During the pre-study period and during the Treatment Period up to 48 weeks

End point values	Certolizumab Pegol (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	89			
Units: flares				
number (confidence interval 95%)				
Pre-study Historical	132.72 (109.76 to 159.06)			
On-study CZP	18.56 (10.39 to 30.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and a history of AU at Week 96

End point title	Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and a history of AU at Week 96

End point description:

A flare was defined as being a new episode of Anterior Uveitis (AU) that, based on the judgment of an ophthalmologist, required specific treatment. A flare was considered a new episode if a gap of at least 3 months occurred between 2 flares.
The Full Analysis Set (FAS) consisted of all study participants in the Safety Set (SS) with nonmissing Baseline values for the primary efficacy variable (AU flare incidence data from the prestudy period).

End point type	Secondary

End point timeframe:

During the pre-study period and during the Treatment Period up to 96 weeks

End point values	Certolizumab Pegol (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	89			
Units: flares				
number (confidence interval 95%)				
Pre-study Historical	97.51 (83.24 to 113.53)			
On-study CZP	17.67 (11.74 to 25.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and at least 1 AU episode within 12 months prior Baseline at Week 48

End point title	Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and at least 1 AU episode within 12 months prior Baseline at Week 48

End point description:

A flare was defined as being a new episode of Anterior Uveitis (AU) that, based on the judgment of an ophthalmologist, required specific treatment. A flare was considered a new episode if a gap of at least 3 months occurred between 2 flares.
The Full Analysis Set (FAS) consisted of all study participants in the Safety Set (SS) with nonmissing Baseline values for the primary efficacy variable (AU flare incidence data from the prestudy period).

End point type	Secondary

End point timeframe:

During the pre-study period and during the Treatment Period up to 48 weeks

End point values	Certolizumab Pegol (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	89			
Units: flares				
number (confidence interval 95%)				
Pre-study Historical	132.72 (109.76 to 159.06)			
On-study CZP	18.56 (10.39 to 30.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and at least 1 AU episode within 12 months prior Baseline at Week 96

End point title	Number of Anterior Uveitis (AU) flares per 100 patient-years in participants with active axial SpondyloArthritis (axSpA) and at least 1 AU episode within 12 months prior Baseline at Week 96

End point description:

A flare was defined as being a new episode of Anterior Uveitis (AU) that, based on the judgment of an ophthalmologist, required specific treatment. A flare was considered a new episode if a gap of at least 3 months occurred between 2 flares.
The Full Analysis Set (FAS) consisted of all study participants in the Safety Set (SS) with nonmissing Baseline values for the primary efficacy variable (AU flare incidence data from the prestudy period).

End point type	Secondary

End point timeframe:

During the pre-study period and during the Treatment Period up to 96 weeks

End point values	Certolizumab Pegol (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	89			
Units: flares				
number (confidence interval 95%)				
Pre-study Historical	97.51 (83.24 to 113.53)			
On-study CZP	17.67 (11.74 to 25.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 48

End point title	Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 48

End point description:

The ASDAS was calculated as the sum of the following:
0.121 × Back pain (BASDAI Question 2 result)
0.058 × Duration of morning stiffness (BASDAI Question 6 result)
0.110 × PtGADA
0.073 × Peripheral pain/swelling (BASDAI Question 3 result)
0.579 × (natural logarithm (CRP [mg/L] + 1))
Back pain, PtGADA, duration of morning stiffness, and peripheral pain/swelling are all assessed on a numerical scale (0 to 10 units).
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
There is a minimum score of 0.636 for the total ASDAS score, but no defined upper score. Based on the formula even in the situation that the CRP is normal, any value below 4 is recorded as BLQ and a value of BLQ/2=2 was prespecified. This assumption is triggering the lowest possible value of 0.636.
The SS consisted of all participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing ASDAS

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-1.55 (± 1.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 96

End point title	Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 96

End point description:

The ASDAS was calculated as the sum of the following:
0.121 × Back pain (BASDAI Question 2 result)
0.058 × Duration of morning stiffness (BASDAI Question 6 result)
0.110 × PtGADA
0.073 × Peripheral pain/swelling (BASDAI Question 3 result)
0.579 × (natural logarithm (CRP [mg/L] + 1))
Back pain, PtGADA, duration of morning stiffness, and peripheral pain/swelling are all assessed on a numerical scale (0 to 10 units).
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
There is a minimum score of 0.636 for the total ASDAS score, but no defined upper score. Based on the formula even in the situation that the CRP is normal, any value below 4 is recorded as BLQ and a value of BLQ/2=2 was prespecified. This assumption is triggering the lowest possible value of 0.636.
The SS consisted of all participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing ASDAS at Week 96

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-1.61 (± 1.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 48

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 48

End point description:

The BASDAI is a validated self-reported instrument which consists of 6 horizontal Numeric Rating Scales (NRSs), each with 10 units to measure the severity of the 5 major symptoms: fatigue, spinal pain, peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration) over the last week. To give each symptom equal weighting, the average of the 2 scores relating to morning stiffness is taken. The resulting 0 to 50 sum score is divided by 5 to give a final BASDAI score between 0 and 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.

Number of participants analyzed reflect those with a non-missing BASDAI at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.2 (± 2.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 96

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 96

End point description:

The BASDAI is a validated self-reported instrument which consists of 6 horizontal Numeric Rating Scales (NRSs), each with 10 units to measure the severity of the 5 major symptoms: fatigue, spinal pain, peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration) over the last week. To give each symptom equal weighting, the average of the 2 scores relating to morning stiffness is taken. The resulting 0 to 50 sum score is divided by 5 to give a final BASDAI score between 0 and 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing BASDAI at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.4 (± 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society 20 % response criteria (ASAS20) at Week 48

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society 20 % response criteria (ASAS20) at Week 48

End point description:

The ASAS20 is defined as an improvement of at least 20 % and absolute improvement of at least 1 unit on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 following domains and absence of deterioration in the potential remaining domain [deterioration was defined as a relative worsening of at least 20 % and an absolute worsening of at least 1 unit]:

- Patient’s Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Percentages were based on the number of participants with an assessment at Week 48.

End point type	Secondary

End point timeframe:

Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	75.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society 20 % response criteria (ASAS20) at Week 96

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society 20 % response criteria (ASAS20) at Week 96

End point description:

The ASAS20 is defined as an improvement of at least 20 % and absolute improvement of at least 1 unit on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 following domains and absence of deterioration in the potential remaining domain [deterioration was defined as a relative worsening of at least 20 % and an absolute worsening of at least 1 unit]:

- Patient’s Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.

Percentages were based on the number of participants with an assessment at Week 96.

End point type	Secondary

End point timeframe:

Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: percentage of participants				
number (not applicable)	75.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society 40 % response criteria (ASAS40) at Week 48

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society 40 % response criteria (ASAS40) at Week 48

End point description:

The ASAS criteria for 40 % improvement were defined as relative improvements of at least 40 %, and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 domains below and no worsening at all in the remaining domain:

- Patient’s Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Percentages were based on the number of participants with an assessment at Week 48.

End point type	Secondary

End point timeframe:

Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	53.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society 40 % response criteria (ASAS40) at Week 96

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society 40 % response criteria (ASAS40) at Week 96

End point description:

The ASAS criteria for 40 % improvement were defined as relative improvements of at least 40 %, and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 domains below and no worsening at all in the remaining domain:

- Patient's Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Percentages were based on the number of participants with an assessment at Week 96.

End point type	Secondary

End point timeframe:

Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: percentage of participants				
number (not applicable)	58.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society (ASAS) 5/6 response at Week 48

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society (ASAS) 5/6 response at Week 48

End point description:

The ASAS 5/6 response is defined as at least 20 % improvement in 5 of 6 domains, including spinal mobility (lateral spinal flexion) and C-Reactive Protein (CRP) as more objective measures.
As the BASMI was not collected, and there was no alternative measure of spinal mobility available in the study data, the complete component for spinal mobility was missing. Therefore the ASAS 5/6 response criterion cannot be calculated, and the analysis of the secondary efficacy variable ASAS 5/6 had to be dropped.

End point type	Secondary

End point timeframe:

Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[1]			
Units: percentage of participants				
number (not applicable)				

Notes:

[1] - Data not collected from participants in all Arms/Groups.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants meeting Assessment of SpondyloArthritis international Society (ASAS) 5/6 response at Week 96

End point title	Percentage of participants meeting Assessment of SpondyloArthritis international Society (ASAS) 5/6 response at Week 96

End point description:

The ASAS 5/6 response is defined as at least 20 % improvement in 5 of 6 domains, including spinal mobility (lateral spinal flexion) and C-Reactive Protein (CRP) as more objective measures.
As the BASMI was not collected, and there was no alternative measure of spinal mobility available in the study data, the complete component for spinal mobility was missing. Therefore the ASAS 5/6 response criterion cannot be calculated, and the analysis of the secondary efficacy variable ASAS 5/6 had to be dropped.

End point type	Secondary

End point timeframe:

Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[2]			
Units: percentage of participants				
number (not applicable)				

Notes:

[2] - Data not collected from participants in all Arms/Groups.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Assessment of SpondyloArthritis international Society (ASAS) partial remission (PR) response at Week 48

End point title	Percentage of participants with Assessment of SpondyloArthritis international Society (ASAS) partial remission (PR) response at Week 48

End point description:

The ASAS PR response is defined as a score of ≤2 units on a 0 to 10 unit scale in all of the 4 following domains:

- Patient’s Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Percentages were based on the number of participants with an assessment at Week 48.

End point type	Secondary

End point timeframe:

Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	31.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Assessment of SpondyloArthritis international Society (ASAS) partial remission (PR) response at Week 96

End point title	Percentage of participants with Assessment of SpondyloArthritis international Society (ASAS) partial remission (PR) response at Week 96

End point description:

The ASAS PR response is defined as a score of ≤2 units on a 0 to 10 unit scale in all of the 4 following domains:

- Patient’s Global Assessment of Disease Activity (PtGADA)
- Pain assessment (the total spinal pain Numeric Rating Scale score)
- Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI))
- Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration)

The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Percentages were based on the number of participants with an assessment at Week 96.

End point type	Secondary

End point timeframe:

Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: percentage of participants				
number (not applicable)	36.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in tender joint count (44 joint count) at Week 48

End point title	Change from Baseline in tender joint count (44 joint count) at Week 48

End point description:

The following 44 joints were to be examined for swelling and tenderness by the Investigator, another delegated physician, or an appropriately qualified medical professional:
- Upper body (4) – bilateral sternoclavicular and acromioclavicular joints
- Upper extremity (26) – bilateral shoulders, elbows, wrists (includes radiocarpal, carpal, and carpometacarpal bones considered as a single unit), metacarpophalangeals (MCPs) I,II, III, IV, and V, and thumb interphalangeals (IPs), and proximal IPs (PIPs) II, III, IV, and V
- Lower extremity (14) – bilateral knees, ankles, and metatarsophalangeals (I, II, III, IV, and V)
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The SS consisted of all study participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with at least one tender joint count at Baseline (N=59) and had a non-missing tender joint count at Week 48 (N=55).

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	55			
Units: tender joints				
arithmetic mean (standard deviation)	-4.9 (± 6.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in tender joint count (44 joint count) at Week 96

End point title	Change from Baseline in tender joint count (44 joint count) at Week 96

End point description:

The following 44 joints were to be examined for swelling and tenderness by the Investigator, another delegated physician, or an appropriately qualified medical professional:
- Upper body (4) – bilateral sternoclavicular and acromioclavicular joints

- Upper extremity (26) – bilateral shoulders, elbows, wrists (includes radiocarpal, carpal, and carpometacarpal bones considered as a single unit), metacarpophalangeals (MCPs) I,II, III, IV, and V, and thumb interphalangeals (IPs), and proximal IPs (PIPs) II, III, IV, and V
- Lower extremity (14) – bilateral knees, ankles, and metatarsophalangeals (I, II, III, IV, and V)
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The SS consisted of all study participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with at least one tender joint count at Baseline (N=59) and had a non-missing tender joint count at Week 96 (N=51).

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: tender joints				
arithmetic mean (standard deviation)	-4.7 (± 8.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in swollen joint count (44 joint count) at Week 48

End point title	Change from Baseline in swollen joint count (44 joint count) at Week 48

End point description:

The following 44 joints were to be examined for swelling and tenderness by the Investigator, another delegated physician, or an appropriately qualified medical professional:
- Upper body (4) – bilateral sternoclavicular and acromioclavicular joints
- Upper extremity (26) – bilateral shoulders, elbows, wrists (includes radiocarpal, carpal, and carpometacarpal bones considered as a single unit), metacarpophalangeals (MCPs) I,II, III, IV, and V, and thumb interphalangeals (IPs), and proximal IPs (PIPs) II, III, IV, and V
- Lower extremity (14) – bilateral knees, ankles, and metatarsophalangeals (I, II, III, IV, and V)
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The SS consisted of all study participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with at least one swollen joint count at Baseline (N=33) and had a non-missing swollen joint count at Week 48 (N=32).

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: swollen joints				
arithmetic mean (standard deviation)	-4.2 (± 4.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in swollen joint count (44 joint count) at Week 96

End point title	Change from Baseline in swollen joint count (44 joint count) at Week 96

End point description:

The following 44 joints were to be examined for swelling and tenderness by the Investigator, another delegated physician, or an appropriately qualified medical professional:
- Upper body (4) – bilateral sternoclavicular and acromioclavicular joints
- Upper extremity (26) – bilateral shoulders, elbows, wrists (includes radiocarpal, carpal, and carpometacarpal bones considered as a single unit), metacarpophalangeals (MCPs) I,II, III, IV, and V, and thumb interphalangeals (IPs), and proximal IPs (PIPs) II, III, IV, and V
- Lower extremity (14) – bilateral knees, ankles, and metatarsophalangeals (I, II, III, IV, and V)
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The SS consisted of all study participants in the ES who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with at least one swollen joint count at Baseline (N=33) and had a non-missing swollen joint count at Week 96 (N=30).

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: swollen joints				
arithmetic mean (standard deviation)	-3.9 (± 5.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician's Global Assessment of Disease Activity (PhGADA) at Week 48

End point title	Change From Baseline in Physician's Global Assessment of Disease Activity (PhGADA) at Week 48

End point description:

The Investigator assessed the overall status of the participant with respect to the axSpA signs and symptoms and the functional capacity of the participant using a Visual Analog Scale (VAS) where 0 is

"very good, asymptomatic and no limitation of normal activities" and 100 is "very poor, very severe symptoms that are intolerable, and the inability to carry out all normal activities."
This assessment by the Investigator should be made without any knowledge of the Patient's Global Assessment of Disease Activity (PtGADA).
Total score ranges from 0 to 100, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing PhGADA at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-43.8 (± 21.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician's Global Assessment of Disease Activity (PhGADA) at Week 96

End point title	Change From Baseline in Physician's Global Assessment of Disease Activity (PhGADA) at Week 96

End point description:

The Investigator assessed the overall status of the participant with respect to the axSpA signs and symptoms and the functional capacity of the participant using a Visual Analog Scale (VAS) where 0 is "very good, asymptomatic and no limitation of normal activities" and 100 is "very poor, very severe symptoms that are intolerable, and the inability to carry out all normal activities."
This assessment by the Investigator should be made without any knowledge of the Patient's Global Assessment of Disease Activity (PtGADA).
Total score ranges from 0 to 100, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing PhGADA at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-42.5 (± 27.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Global Assessment of Disease Activity (PtGADA) at Week 48

End point title	Change From Baseline in Patient's Global Assessment of Disease Activity (PtGADA) at Week 48

End point description:

For the PtGADA questionnaire, participants scored their global assessment of their disease activity in response to the question "How active was your spondylitis on average during the last week?" using a Numeric Rating Scale (NRS) where 0 was "not active" and 10 was "very active".
Total score ranges from 0 to 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing PtGADA at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.6 (± 2.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Global Assessment of Disease Activity (PtGADA) at Week 96

End point title	Change From Baseline in Patient's Global Assessment of Disease Activity (PtGADA) at Week 96

End point description:

For the PtGADA questionnaire, participants scored their global assessment of their disease activity in response to the question "How active was your spondylitis on average during the last week?" using a Numeric Rating Scale (NRS) where 0 was "not active" and 10 was "very active".

Total score ranges from 0 to 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing PtGADA at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.9 (± 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total spinal pain at Week 48 assessed by Numerical Rating Scale (NRS)

End point title	Change from Baseline in total spinal pain at Week 48 assessed by Numerical Rating Scale (NRS)

End point description:

The total spinal pain was assessed with the question 'How much pain of your spine due to spondylitis do you have?' using a Numeric Rating Scale (NRS) where 0 was 'No pain' and 10 was 'Most severe pain'. Usually, a 10 % difference (ie, a 1 point difference on a Numeric Rating Scale (NRS) ranging from 0 to 10) is considered the minimal clinically important difference used to interpret scores (Dworkin et al, 2008).
Total score ranges from 0 to 10, with lower scores indicating a worse outcome.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing total spinal pain assessment at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.8 (± 2.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total spinal pain at Week 96 assessed by Numerical Rating Scale (NRS)

End point title	Change from Baseline in total spinal pain at Week 96 assessed by Numerical Rating Scale (NRS)

End point description:

The total spinal pain was assessed with the question 'How much pain of your spine due to spondylitis do you have?' using a Numeric Rating Scale (NRS) where 0 was 'No pain' and 10 was 'Most severe pain'. Usually, a 10 % difference (ie, a 1 point difference on a Numeric Rating Scale (NRS) ranging from 0 to 10) is considered the minimal clinically important difference used to interpret scores (Dworkin et al, 2008).
Total score ranges from 0 to 10, with lower scores indicating a worse outcome.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing total spinal pain assessment at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-4.1 (± 2.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 48 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point title	Change from Baseline to Week 48 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point description:

The BASFI is a validated disease-specific instrument for assessing physical function (van Tubergen et al, 2015; Calin et al, 1994; van der Heijde et al, 2005).
The BASFI comprises 10 items relating to the past week. The Numeric Rating Scale (NRS) version was used for the answering options of each item on a scale of 0 (“Easy”) to 10 (“Impossible”) (van Tubergen

et al, 2002). The BASFI score is the mean of the 10 items such that the total score ranges from 0 to 10, with lower scores indicating better physical function.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing BASFI at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-2.23 (± 2.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 96 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point title	Change from Baseline to Week 96 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point description:

The BASFI is a validated disease-specific instrument for assessing physical function (van Tubergen et al, 2015; Calin et al, 1994; van der Heijde et al, 2005).
The BASFI comprises 10 items relating to the past week. The Numeric Rating Scale (NRS) version was used for the answering options of each item on a scale of 0 ("Easy") to 10 ("Impossible") (van Tubergen et al, 2002). The BASFI score is the mean of the 10 items such that the total score ranges from 0 to 10, with lower scores indicating better physical function.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing BASFI at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-2.28 (± 2.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 48 in Inflammation assessed by the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness and duration

End point title	Change from Baseline to Week 48 in Inflammation assessed by the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness and duration

End point description:

The BASDAI is a validated self-reported instrument which consists of six 10-unit horizontal Numeric Rating Scales (NRS) to measure severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration for each disease activity, respectively) over the last week. The mean of the 2 BASDAI questions related to morning stiffness (questions 5 and 6) ranged from 0 to 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing BASDAI at Week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.7 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 96 in Inflammation assessed by the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness and duration

End point title	Change from Baseline to Week 96 in Inflammation assessed by the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness and duration

End point description:

The BASDAI is a validated self-reported instrument which consists of six 10-unit horizontal Numeric Rating Scales (NRS) to measure severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration for each disease activity, respectively) over the last week. The mean of the 2 BASDAI questions related to morning stiffness (questions 5 and 6) ranged from 0 to 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.
Number of participants analyzed reflect those with a non-missing BASDAI at Week 96.

End point type	Secondary

End point timeframe:

From Baseline to Week 96

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	82			
Units: scores on a scale				
arithmetic mean (standard deviation)	-3.8 (± 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting at least one Treatment-Emergent Adverse Events (TEAEs) during the study

End point title	Percentage of participants reporting at least one Treatment-Emergent Adverse Events (TEAEs) during the study

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
The Safety Set consisted of all study participants in the Enrolled Set who had received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From Baseline up to the Safety Follow-up Visit (up to Week 104)

End point values	Certolizumab Pegol (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	89			
Units: percentage of participants				
number (not applicable)	80.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected from Baseline to the Safety Follow-up Visit (up to Week 104)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Certolizumab Pegol (SS)

Reporting group description:

Participants received a loading dose of Certolizumab Pegol (CZP) 400 mg subcutaneously (sc) administered at Baseline, Week 2, and Week 4 followed by CZP 200 mg sc Q2W (starting at Week 6 until Week 94).

Serious adverse events	Certolizumab Pegol (SS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 89 (12.36%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemangioma			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Incarcerated hernia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal polyp			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Tenosynovitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia haemophilus			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Certolizumab Pegol (SS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 89 (57.30%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 89 (5.62%)		
occurrences (all)	5		
Eye disorders			
Uveitis			
subjects affected / exposed	14 / 89 (15.73%)		
occurrences (all)	23		
Iridocyclitis			
subjects affected / exposed	8 / 89 (8.99%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 89 (5.62%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	6 / 89 (6.74%) 7		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all)	 15 / 89 (16.85%) 22 12 / 89 (13.48%) 15 6 / 89 (6.74%) 9 6 / 89 (6.74%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2017	Global Protocol Amendment 2 (dated 17 Jan 2017) was a substantial protocol amendment implemented to provide clarification on Magnetic Resonance Imaging (MRI) and x-ray assessments. In addition, information concerning the collection of data for the assessment of Anterior Uveitis (AU) flares and information concerning Hy's Law cases was added. Other minor updates/clarifications were also made. Details of global changes are provided below: • Clarification was added that if no chest x-ray was available within the 3 months prior to Screening, the x-ray could be done during the Screening Period. If the modified New York (mNY) classification criteria were met in the x-ray performed prior to Screening, the x-ray was not to be repeated. • Clarification was added that an MRI assessment was not needed for study participants with Ankylosing Spondylitis (AS) and that AS study participants were to have evidence of sacroiliitis on x-ray taken prior to Baseline, meeting the mNY classification criteria according to the Investigator. • Minor updates were made to ophthalmic exclusion criteria and prior concomitant medications exclusion table. • Minor edits were made to text concerning storage conditions at the site. • Details about the information collected for the assessment of AU flares were added. • Information concerning Hy's Law cases was added to the Adverse Events (AEs) of Interest section. • Minor corrections were made globally.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported