



Clinical trial results:

A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Ustekinumab in the Treatment of Subjects With Active Nonradiographic Axial Spondyloarthritis

Summary

EudraCT number	2015-000289-67
Trial protocol	BE HU DE CZ
Global end of trial date	26 September 2017

Results information

Result version number	v1 (current)
This version publication date	12 October 2018
First version publication date	12 October 2018

Trial information

Trial identification

Sponsor protocol code	CNT01275AKS3003
-----------------------	-----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02407223
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333 CM
Public contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 September 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the efficacy of ustekinumab in adult subjects with active nr-AxSpA, measured by the reduction in signs and symptoms of nr-AxSpA.

Protection of trial subjects:

Safety was evaluated based on adverse events (AEs), clinical laboratory tests, vital sign measurements, physical examinations, ECGs (screening only), concomitant medication review, injection-site reactions, allergic reactions, infections, and tuberculosis (TB) evaluations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Australia: 22
Country: Number of subjects enrolled	Belgium: 27
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Russian Federation: 62
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	Ukraine: 57
Worldwide total number of subjects	356
EEA total number of subjects	150

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)	356
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 356 subjects were randomized and received treatment (116 subjects to placebo, 118 subjects to ustekinumab 45 milligram [mg], and 122 subjects to 90 mg).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo SC at Week(W) 0, 4, 16 and 20. At W16, subjects in placebo group who qualified for early escape (EE) criteria (with <10 percent (%) improvement from baseline in both total back pain and morning stiffness measures at Week 12 and 16) were re-randomized to receive ustekinumab 45mg or 90mg at W 16, 20,28 followed by q12w dosing through W52. Subjects received placebo SC at W24 to maintain the blind. At W24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at W24, 28 followed by q12w therapy through W52. At W52, subjects who achieved inactive disease (Ankylosing Spondylitis Disease Activity Score [ASDAS] [ESR]<1.3) at W40,52 underwent re-randomization to either ustekinumab or placebo. Subjects who did not achieve inactive disease either W40 or 52 received previously assigned ustekinumab dose at scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo SC injection at Weeks 0, 4, 16 and 20.

Investigational medicinal product name	Ustekinumab 45 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

At Week 16, subjects in placebo group who qualified for EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at Weeks 16, 20 and 28 followed by q12w dosing through Week 52. At Week 24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at Week 24 and 28 followed by q12w therapy through Week 52. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits.

Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

At Week 16, subjects in placebo group who qualified for EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at Weeks 16, 20 and 28 followed by q12w dosing through Week 52. At Week 24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at Week 24 and 28 followed by q12w therapy through Week 52. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits.

Arm title	Ustekinumab 45mg
------------------	------------------

Arm description:

Subjects received ustekinumab 45 mg subcutaneously (SC) at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR less than [$<$]1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab 45mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received ustekinumab 45 mg SC at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind.

Arm title	Ustekinumab 90mg
------------------	------------------

Arm description:

Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab 90mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind.

Number of subjects in period 1	Placebo	Ustekinumab 45mg	Ustekinumab 90mg
Started	116	118	122
Early Escape at Week 16	22	0	0
Cross over at Week 24	60	0	0
Qualified Re-randomization at Week 52	0	3	2
Completed	0	0	0
Not completed	116	118	122
Consent withdrawn by subject	2	4	4
Adverse event	1	-	1
Study terminated by sponsor	77	80	86
Unspecified	29	27	25
Lost to follow-up	1	-	2
Subject refused further study treatment	-	1	-
Lack of efficacy	6	6	4

Baseline characteristics

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Subjects received placebo SC at Week(W) 0, 4, 16 and 20. At W16, subjects in placebo group who qualified for early escape (EE) criteria (with <10 percent (%) improvement from baseline in both total back pain and morning stiffness measures at Week 12 and 16) were re-randomized to receive ustekinumab 45mg or 90mg at W 16, 20,28 followed by q12w dosing through W52. Subjects received placebo SC at W24 to maintain the blind. At W24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at W24, 28 followed by q12w therapy through W52. At W52, subjects who achieved inactive disease (Ankylosing Spondylitis Disease Activity Score [ASDAS] [ESR]<1.3) at W40,52 underwent re-randomization to either ustekinumab or placebo. Subjects who did not achieve inactive disease either W40 or 52 received previously assigned ustekinumab dose at scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Reporting group title	Ustekinumab 45mg
-----------------------	------------------

Reporting group description:

Subjects received ustekinumab 45 mg subcutaneously (SC) at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR less than [<]1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Reporting group title	Ustekinumab 90mg
-----------------------	------------------

Reporting group description:

Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.

Reporting group values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg
Number of subjects	116	118	122
Title for AgeCategorical Units: subjects			
<30	40	45	39
>=30	76	73	83
Title for AgeContinuous Units: years			
arithmetic mean	34	33.9	34.9
standard deviation	± 8.75	± 8.39	± 9.06
Title for Gender Units: subjects			
Female	52	65	59
Male	64	53	63

Reporting group values	Total		
Number of subjects	356		
Title for AgeCategorical Units: subjects			
<30	124		
>=30	232		

Title for AgeContinuous Units: years arithmetic mean standard deviation	-		
Title for Gender Units: subjects			
Female	176		
Male	180		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received placebo SC at Week(W) 0, 4, 16 and 20. At W16, subjects in placebo group who qualified for early escape (EE) criteria (with <10 percent (%) improvement from baseline in both total back pain and morning stiffness measures at Week 12 and 16) were re-randomized to receive ustekinumab 45mg or 90mg at W 16, 20,28 followed by q12w dosing through W52. Subjects received placebo SC at W24 to maintain the blind. At W24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at W24, 28 followed by q12w therapy through W52. At W52, subjects who achieved inactive disease (Ankylosing Spondylitis Disease Activity Score [ASDAS] [ESR]<1.3) at W40,52 underwent re-randomization to either ustekinumab or placebo. Subjects who did not achieve inactive disease either W40 or 52 received previously assigned ustekinumab dose at scheduled visits. Last dose was scheduled for W88 and last study visit for W100.	
Reporting group title	Ustekinumab 45mg
Reporting group description: Subjects received ustekinumab 45 mg subcutaneously (SC) at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR less than [<]1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.	
Reporting group title	Ustekinumab 90mg
Reporting group description: Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. Last dose was scheduled for W88 and last study visit for W100.	

Primary: Percentage of Subjects Who Achieved Assessment of SpondyloArthritis International Society (ASAS) 20 Response at Week 24

End point title	Percentage of Subjects Who Achieved Assessment of SpondyloArthritis International Society (ASAS) 20 Response at Week 24
End point description: ASAS20:>=20% improvement and absolute improvement from baseline of 1 on 0-10 cm scale in at least 3 of following: PGA disease activity(0-10 cm; 0=very well,10=very poor), total back pain(0-10 cm; 0=no pain,10=most severe pain), BASFI (self-assessment given as mean [0-10cm; 0=easy, 10=impossible]) of 10 questions, 8 relates to functional anatomy and 2 to ability to cope with everyday life), Inflammation(0-10cm;0=none,10=very severe); absence of deterioration(>=20% and worsening of at least 1 on 0-10 cm scale) in remaining domain. ASAS20 response based on imputed data using treatment failure (consider non-responders[NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NRI(missing responses at post baseline visit imputed as NRI). MFAS-subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment received.	
End point type	Primary
End point timeframe: Week 24	

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)	47.6	55.4	49.4	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Ustekinumab 45mg
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.232
Method	CMH chi-square test
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	23.1

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v Ustekinumab 90mg
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.876
Method	CMH chi-square test
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	17

Secondary: Percentage of Subjects Who Achieved an ASAS 40 Response at Week 24

End point title	Percentage of Subjects Who Achieved an ASAS 40 Response at Week 24
-----------------	--

End point description:

ASAS40: $\geq 40\%$ improvement and absolute improvement from baseline of at least 2 on 0-10 cm scale in at least 3 of following: PGA of disease activity (0-10 cm; 0=very well,10=very poor),total back pain (0-10 cm; 0=no pain,10=most severe pain), BASFI (self-assessment given as mean (0-10 cm; 0=easy to 10=impossible) of 10 questions, 8 of which relate to functional anatomy and 2 to subjects ability to cope with everyday life), Inflammation (0-10 cm;0=none,10=very severe); no worsening at all in remaining domain. ASAS40 response based on imputed data using treatment failure (consider non-responders [NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NRI (missing responses at post baseline visit imputed as NR). MFAS- subjects who were randomized (those

who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received.

End point type	Secondary
End point timeframe:	
Week 24	

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)	25.6	33.7	28.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved at Least a 50% Improvement From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 24

End point title	Percentage of Subjects Who Achieved at Least a 50% Improvement From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 24
-----------------	--

End point description:

BASDAI consists of 6 questions: fatigue, spinal pain, arthralgia/swelling, enthesitis and morning stiffness (2 questions: duration and severity). Each question to answer 10cm visual analog scale (VAS), with 0=none, and 10=very severe. To give each of 5 symptoms equal weight, mean of 2 questions about morning stiffness were added to total of the remaining 4 scores and final BASDAI score (ranging 0-10) is average of overall total score. Higher score indicates more severe AS symptom. 50% improvement in response based on imputed data using treatment failure (consider non-responders [NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NR imputation (missing responses at post baseline visit imputed as NR). MFAS- subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received.

End point type	Secondary
End point timeframe:	
Week 24	

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)	23.2	32.5	25.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 24

End point title	Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 24
-----------------	---

End point description:

BASFI- composed with 10 questions (each question is answered with a VAS 0-10 cm) to assess disease severity, including first 8 questions regarding to functional anatomy related activities and the 2 questions related to daily activities of AS subjects. Each question is a 10 cm VAS with a value between 0 (easy) and 10 (impossible). Final BASFI score is mean of 10 scores. BASFI score is average of 10 responses and has a possible minimum value of 0 and maximum value of 10. Higher score indicates more severe functional limitations of the subject due to AS. Early escape rule was applied (measurement value at Week 20 and Week 24 was set as missing). MFAS- subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received. 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 24

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	72	63	
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.11 (\pm 2.371)	-2.28 (\pm 2.625)	-1.90 (\pm 2.731)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Ankylosing Spondylitis Disease Activity Score (ASDAS) C-reactive protein (CRP) Inactive Disease (<1.3) at Week 24

End point title	Percentage of Subjects who Achieved Ankylosing Spondylitis Disease Activity Score (ASDAS) C-reactive protein (CRP) Inactive Disease (<1.3) at Week 24
-----------------	---

End point description:

ASDAS: CRP (mg/L) with 4 items (on 0-10 cm VAS or 0-10 numerical rating scale [NRS]) having total back pain, duration of morning stiffness, peripheral pain/swelling and PGA. ASDAS scores- $ASDAS(CRP) = (0.121 * \text{total back pain}) + (0.110 * \text{subject global}) + (0.073 * \text{peripheral pain/swelling}) + (0.058 * \text{duration of morning stiffness}) + (0.579 * \ln(CRP + 1))$. Disease activity, TBP and peripheral pain/swelling on NRS (0 [normal] to 10 [very severe] and DMS on NRS (0-10, 0=none, 10=duration of ≥ 2 hours). Inactive disease- an ASDAS score <1.3. ASDAS (CRP). It is based on imputed data using treatment failure(consider non-responders [NR] at and after treatment failure), EE rules(consider NR at W 20 and 24), NR imputation(missing responses at post baseline imputed as NR). MFAS-subjects who randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received atleast 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	85	85	
Units: Percentage of subjects				
number (not applicable)	7.3	14.5	12.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) Levels Through Week 24

End point title	Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) Levels Through Week 24
-----------------	--

End point description:

Change from baseline in hsCRP levels was reported. hsCRP is a sensitive laboratory assay for serum levels of C-Reactive Protein, which is a biomarker of inflammation. Missing values were imputed using early escape rule (measurement value at Week 20 and Week 24 was set as missing). MFAS-subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received. Here 'n'-number of subjects who were analyzed at each specified timepoints, for each arm, respectively.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20 and 24

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Change at Week 4(n=82,83,84)	-0.08 (± 1.567)	-0.10 (± 2.574)	-0.39 (± 1.601)	
Change at Week 8(n=82,82,82)	-0.23 (± 1.490)	-0.53 (± 2.084)	-0.57 (± 2.209)	
Change at Week 12(n=80,81,81)	-0.23 (± 1.661)	-0.71 (± 2.392)	-0.61 (± 2.534)	
Change at Week 16(n=79,82,80)	-0.49 (± 1.725)	-0.63 (± 2.21)	-0.61 (± 2.539)	
Change at Week 20(n=61,80,80)	-0.36 (± 1.951)	-0.78 (± 2.353)	-0.76 (± 2.383)	
Change at Week 24(n=62,79,79)	-0.42 (± 2.145)	-0.63 (± 2.402)	-0.78 (± 2.413)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With ASAS 20 Components at Week 24

End point title	Percentage of Subjects With ASAS 20 Components at Week 24
-----------------	---

End point description:

ASAS 20 defined as $\geq 20\%$ improvement from baseline in 4 individual components of ASAS20: Patient's global assessment (PGA) of disease activity (0 to 10cm; 0=very well,10=very poor),total back pain(0 to 10cm; 0=no pain,10=most severe pain), BASFI (self-assessment represented as mean(0 to 10 cm; 0=easy to 10=impossible) of 10 questions, 8 of which relate to functional anatomy and 2 relate to subjects ability to cope with life) and Inflammation (0 to 10cm;0=none,10=very severe). MFAS-subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received. 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	80	80	
Units: Percentage of subjects				
number (not applicable)				
$\geq 20\%$ improvement from baseline in PGA score	64.1	61.3	58.8	
$\geq 20\%$ improvement from baseline in total back pain	62.8	60.0	60.0	
$\geq 20\%$ improvement from baseline in BASFI	53.8	57.5	56.3	
$\geq 20\%$ improvement from baseline in inflammation	64.1	66.3	65.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved ASAS 40 Response at Week 4, 8, 12, 16 and 20

End point title	Percentage of Subjects Who Achieved ASAS 40 Response at Week 4, 8, 12, 16 and 20
-----------------	--

End point description:

ASAS40: $\geq 40\%$ improvement and absolute improvement from baseline of at least 2 on 0-10 cm scale in at least 3 of following: PGA of disease activity (0-10 cm; 0=very well,10=very poor),total back pain (0-10 cm; 0=no pain,10=most severe pain), BASFI (self-assessment given as mean (0-10 cm; 0=easy to 10=impossible) of 10 questions, 8 of which relate to functional anatomy and 2 to subjects ability to cope with everyday life), Inflammation (0-10 cm;0=none,10=very severe); no worsening at all in remaining domain. ASAS40 response based on imputed data using treatment failure (consider non-responders [NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NRI (missing responses at post baseline visit imputed as NR). MFAS- subjects who were randomized (those who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 4 ,8 ,12 ,16 and 20

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)				
Week 4	3.7	8.4	11.8	
Week 8	18.3	19.3	18.8	
Week 12	17.1	27.7	24.7	
Week 16	19.5	27.7	24.7	
Week 20	24.4	38.6	32.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved ASAS 20 Response at Week 4, 8, 12, 16 and 20

End point title	Percentage of Subjects Who Achieved ASAS 20 Response at Week 4, 8, 12, 16 and 20
-----------------	--

End point description:

ASAS20: $\geq 20\%$ improvement and absolute improvement from baseline of 1 on 0-10 cm scale in at least 3 of following: PGA disease activity(0-10 cm; 0=very well,10=very poor), total back pain(0-10 cm; 0=no pain,10=most severe pain), BASFI (self-assessment given as mean [0-10cm; 0=easy, 10=impossible]) of 10 questions, 8 relates to functional anatomy and 2 to ability to cope with everyday life), Inflammation(0-10cm;0=none,10=very severe); absence of deterioration($\geq 20\%$ and worsening of at least 1 on 0-10 cm scale) in remaining domain. ASAS20 response based on imputed data using treatment failure (consider non-responders[NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NRI(missing responses at post baseline visit imputed as NRI). MFAS-subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment received.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 4, 8, 12, 16 and 20

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)				
Week 4	23.2	26.5	32.9	
Week 8	31.7	41.0	36.5	
Week 12	34.1	48.2	41.2	
Week 16	40.2	49.4	35.3	
Week 20	45.1	59.0	44.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved at Least a 50% Improvement From Baseline in BASDAI at Week 4, 8, 12, 16 and 20

End point title	Percentage of Subjects Who Achieved at Least a 50% Improvement From Baseline in BASDAI at Week 4, 8, 12, 16 and 20
-----------------	--

End point description:

BASDAI consists of 6 questions: fatigue, spinal pain, arthralgia/swelling, enthesitis and morning stiffness (2 questions: duration and severity). Each question to answer 10cm visual analog scale (VAS), with 0=none, and 10=very severe. To give each of 5 symptoms equal weight, mean of 2 questions about morning stiffness were added to total of the remaining 4 scores and final BASDAI score (ranging 0-10) is average of overall total score. Higher score indicates more severe AS symptom. 50% improvement in response based on imputed data using treatment failure (consider non-responders [NR] at and after treatment failure), EE rules (consider NR at Week 20 and 24), NR imputation (missing responses at post baseline visit imputed as NR). MFAS- subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 4, 8, 12, 16, and 20

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)				
Week 4	4.9	8.4	8.2	
Week 8	9.8	15.7	17.6	
Week 12	18.3	16.9	28.2	
Week 16	19.5	21.7	24.7	

Week 20	15.9	28.9	32.9	
Week 24	23.2	33.7	25.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 4, 8, 12, 16 and 20

End point title	Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 4, 8, 12, 16 and 20
End point description:	
BASFI is composed of 10 questions (each answered on VAS 0-10 cm) to assess disease severity, first 8 questions regarding to functional anatomy related activities and other 2 questions related to daily activities. Each question is a 10cm VAS with a value between 0 (easy) and 10 (impossible). Final BASFI score is mean of 10 scores. BASFI score is average of 10 responses and has a possible minimum value of 0 and a possible maximum value of 10. Higher BASFI score indicates more severe functional limitations of the subject due to AS. Early escape rule was applied (measurement value at Week 20 and Week 24 was set as missing). MFAS-subjects who were randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received at least 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment received. 'n' defined as number of subjects who were analyzed at each specified timepoints, for each arm respectively.	
End point type	Secondary
End point timeframe:	
Baseline, Week 4, 8, 12, 16 and 20	

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 4	-0.60 (± 1.582)	-1.15 (± 1.748)	-0.79 (± 1.600)	
Change at Week 8	-0.82 (± 1.997)	-1.54 (± 2.117)	-1.05 (± 2.095)	
Change at Week 12	-1.00 (± 2.064)	-1.69 (± 2.079)	-1.35 (± 2.458)	
Change at Week 16	-1.05 (± 2.162)	-1.75 (± 2.312)	-1.17 (± 2.747)	
Change at Week 20	-1.70 (± 2.339)	-2.11 (± 2.394)	-1.64 (± 2.794)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ASDAS (CRP) Inactive Disease (<1.3) at Week 4, 8, 12, 16, and 20

End point title	Percentage of Subjects with ASDAS (CRP) Inactive Disease (<1.3) at Week 4, 8, 12, 16, and 20
End point description: ASDAS: CRP (mg/L) with 4 items (on 0-10cm VAS or 0-10 numerical rating scale [NRS]) having total back pain, duration of morning stiffness, peripheral pain/swelling and PGA. ASDAS scores- ASDAS(CRP)=(0.121*total back pain)+(0.110*subject global)+(0.073*peripheral pain/swelling)+(0.058*duration of morning stiffness)+ (0.579*Ln(CRP+1). Disease activity, TBP and peripheral pain/swelling on NRS (0 [normal] to 10 [very severe] and DMS on NRS (0-10, 0=none, 10-duration of =>2 hours). Inactive disease- an ASDAS score <1.3. ASDAS (CRP). It is based on imputed data using treatment failure(consider non-responders [NR] at and after treatment failure), EE rules(consider NR at Week 20 and 24), NR imputation(missing responses at post baseline imputed as NR). MFAS-subjects who randomized (those subjects who would have been able to complete Week 24 at time of study discontinuation) and received atleast 1 dose of study drug. Subjects were analyzed per assigned treatment regardless of actual treatment.	
End point type	Secondary
End point timeframe: Week 4, 8, 12, 16, and 20	

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	83	85	
Units: Percentage of subjects				
number (not applicable)				
Week 4	2.4	3.6	1.2	
Week 8	6.1	7.2	9.4	
Week 12	4.1	4.8	10.6	
Week 16	6.1	7.2	11.8	
Week 20	3.7	13.3	15.3	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately up to 2.2 years

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20.0
--------------------	------

Reporting groups

Reporting group title	Placebo Only
-----------------------	--------------

Reporting group description:

Subjects received placebo SC at Week 0, 4, 16 and 20. At Week 16, subjects in placebo group who qualified for EE criteria (with <10 % improvement from baseline in both total back pain and morning stiffness measures at Week 12 and 16) were re-randomized to receive ustekinumab 45mg or 90mg at Weeks 16, 20 and 28 followed by q12w dosing through Week 52. Subjects received placebo SC at W24 to maintain the blind. At Week 24, all remaining subjects in placebo group who did not meet EE criteria were re-randomized to receive ustekinumab 45mg or 90mg at Week 24 and 28 followed by q12w therapy through Week 52. At Week 52, all subjects who achieved inactive disease (ASDAS [ESR]<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits.

Reporting group title	Placebo to Ustekinumab 45mg
-----------------------	-----------------------------

Reporting group description:

Subjects randomized to placebo SC at Week 0 and re-randomized to early escape at Week 16 or cross over at Week 24 to ustekinumab 45 mg SC; adverse events are counted from crossover onward. All subjects regardless qualified for re-randomization at Week 52 or not were counted.

Reporting group title	Placebo to Ustekinumab 90mg
-----------------------	-----------------------------

Reporting group description:

Subjects randomized to placebo SC at week 0 and re-randomized to early escape at Week 16 or cross over at Week 24 to ustekinumab 90 mg SC; adverse events are counted from crossover onward. All subjects regardless qualified for re-randomization at Week 52 or not were counted.

Reporting group title	Ustekinumab 45mg Only
-----------------------	-----------------------

Reporting group description:

Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every 12 weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either Ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. All subjects regardless qualified for re-randomization at Week 52 or not were counted.

Reporting group title	Ustekinumab 90mg Only
-----------------------	-----------------------

Reporting group description:

Subjects received ustekinumab 90 mg subcutaneously at Weeks 0 and 4, followed by every four weeks through Week 52. At Weeks 20 and 24, subjects received placebo subcutaneously to maintain the blind. At Week 52, all subjects who achieved inactive disease (ASDAS ESR<1.3) at both Week 40 and 52 underwent re-randomization to either remain on ustekinumab or placebo. Subjects who did not achieve inactive disease at either Week 40 or 52 received previously assigned ustekinumab dose at their scheduled visits. All subjects regardless qualified for re-randomization at Week 52 or not were counted.

Serious adverse events	Placebo Only	Placebo to Ustekinumab 45mg	Placebo to Ustekinumab 90mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 116 (1.72%)	0 / 42 (0.00%)	2 / 40 (5.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 116 (0.86%)	0 / 42 (0.00%)	0 / 40 (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
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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			
Haemorrhagic Ovarian Cyst			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Menorrhagia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Psychiatric disorders			
Panic Attack			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Axial Spondyloarthritis			
subjects affected / exposed	1 / 116 (0.86%)	0 / 42 (0.00%)	0 / 40 (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
Spondyloarthropathy			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	1 / 40 (2.50%)
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			
Chronic Sinusitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Gastroenteritis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 42 (0.00%)	0 / 40 (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	Ustekinumab 45mg Only	Ustekinumab 90mg Only	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 118 (1.69%)	6 / 122 (4.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	1 / 118 (0.85%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Inguinal Hernia			
subjects affected / exposed	1 / 118 (0.85%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Haemorrhagic Ovarian Cyst			
subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Panic Attack			
subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Axial Spondyloarthritis			
subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			
subjects affected / exposed	0 / 118 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Chronic Sinusitis			

subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 118 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo Only	Placebo to Ustekinumab 45mg	Placebo to Ustekinumab 90mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 116 (16.38%)	4 / 42 (9.52%)	12 / 40 (30.00%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 116 (2.59%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	4	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 116 (0.86%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 116 (1.72%)	0 / 42 (0.00%)	4 / 40 (10.00%)
occurrences (all)	3	0	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 116 (0.86%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	2	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 116 (1.72%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	3
Back Pain			

subjects affected / exposed occurrences (all)	2 / 116 (1.72%) 2	1 / 42 (2.38%) 1	3 / 40 (7.50%) 4
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 116 (0.86%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 116 (4.31%)	2 / 42 (4.76%)	2 / 40 (5.00%)
occurrences (all)	6	2	2
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 116 (5.17%)	1 / 42 (2.38%)	1 / 40 (2.50%)
occurrences (all)	6	1	1

Non-serious adverse events	Ustekinumab 45mg Only	Ustekinumab 90mg Only	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 118 (22.88%)	27 / 122 (22.13%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	5 / 118 (4.24%)	4 / 122 (3.28%)	
occurrences (all)	6	4	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 118 (2.54%)	4 / 122 (3.28%)	
occurrences (all)	6	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 118 (0.85%)	2 / 122 (1.64%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 118 (1.69%)	2 / 122 (1.64%)	
occurrences (all)	2	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 118 (0.85%)	3 / 122 (2.46%)	
occurrences (all)	1	4	

Back Pain subjects affected / exposed occurrences (all)	2 / 118 (1.69%) 2	3 / 122 (2.46%) 4	
Infections and infestations			
Sinusitis subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0	0 / 122 (0.00%) 0	
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	5 / 118 (4.24%) 5	8 / 122 (6.56%) 8	
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	11 / 118 (9.32%) 12	9 / 122 (7.38%) 10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 May 2017	This study was discontinued due to lack of efficacy of either 45 mg or 90 mg dose of ustekinumab observed in the CNTO1275AKS3001 study.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was discontinued before it was fully enrolled, therefore, the interpretation of the efficacy data is limited.

Notes: