Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Ustekinumab in the Treatment of Anti-TNF Refractory Subjects With Active Radiographic Axial Spondyloarthritis

Summary

EudraCT number	2015-000288-16
Trial protocol	HU DE ES CZ BE PL BG GB PT
Global end of trial date	31 August 2017

Results information

Result version number	v1 (current)
This version publication date	15 September 2018
First version publication date	15 September 2018

Trial information

Trial identification

Sponsor protocol code	CNTO1275AKS3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02438787
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	31 August 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 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 antitumor necrosis factor alpha (TNFα) refractory subjects with active radiographic axial spondyloarthritis (AxSpA), as measured by the reduction in signs and symptoms of radiographic AxSpA.

Protection of trial subjects:

Safety was evaluated based on adverse events (AEs), clinical laboratory tests, vital sign measurements, physical examinations, electrocardiograms (ECGs, screening only), concomitant medication review, injection-site reactions, allergic reactions, infections, and tuberculosis (TB) evaluations. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 August 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: 7
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Mexico: 22
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Russian Federation: 69
Country: Number of subjects enrolled	Taiwan: 29
Country: Number of subjects enrolled	Ukraine: 66

Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	315
EEA total number of subjects	88

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)	306
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 315 subjects were randomized and treated (104 subjects to placebo, 106 subjects to ustekinumab 45 milligram (mg), and 105 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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo subcutaneous (SC) injection at Weeks 0, 4, and 16. At Week (W) 16, subjects who met early escape (EE) criteria (less than [<] 10 percent [%] improvement from baseline in both total back pain and morning stiffness measures at both Week 12 and Week 16) were administered open-label golimumab 50 mg SC administrations at Week 16 and every 4 weeks (q4w) thereafter through Week 52. At Week 24 all subjects (with the exception of subjects who qualified for EE) were re-randomized to receive either ustekinumab 45 or 90 mg SC injection at Weeks 24 and 28 followed by every 12 weeks (q12w) dosing, with the last administration of study agent at Week 52.

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, and 16.

Investigational medicinal product name	Golimumab
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 golimumab 50 mg SC administrations at Week 16 and every 4 weeks (q4w) thereafter through Week 52.

Investigational medicinal product name	Ustekinumab 45 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:

Subjects (with the exception of subjects who qualified for EE) were re-randomized and received ustekinumab 45 mg at Weeks 24 and 28 followed by q12w dosing, with the last administration of study agent at Week 52.

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:

Subjects (with the exception of subjects who qualified for EE) were re-randomized and received ustekinumab 90 mg at Weeks 24 and 28 q12w dosing, with the last administration of study agent at Week 52.

Arm title	Ustekinumab 45mg

Arm description:

Subjects received ustekinumab 45 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects were to receive placebo SC injection to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab
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 injection at Weeks 0, 4, and 16, followed by q12w dosing, with the last administration of study agent at Week 52.

Investigational medicinal product name	Golimumab
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 golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52.

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 to maintain the blind at Week 24.

Arm title	Ustekinumab 90mg

Arm description:

Subjects received Ustekinumab 90 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, Subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects received placebo SC injection to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab
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 SC injection at Weeks 0, 4 followed by q12w dosing, with the last administration of study agent at Week 52.

Investigational medicinal product name	Golimumab
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 golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52.

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

Dosage and administration details:

Subjects received placebo SC injection to maintain the blind at Week 24.

Number of subjects in period 1	Placebo	Ustekinumab 45mg	Ustekinumab 90mg
Started	104	106	105
Early escape at week 16	21 [1]	21 [2]	20 [3]
Cross over at week 24	43	0 [4]	0 [5]
Completed	23	23	22
Not completed	81	83	83
Consent withdrawn by subject	15	7	10
Site terminated by sponsor	-	-	1
Adverse event	1	-	2
Unspecified	-	1	-
Lost to follow-up	-	1	-
Study discontinued by sponsor	64	72	69
Lack of efficacy	1	2	-
Protocol deviation	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects who did not met EE criteria at W16 were crossed over to Ustekinumab 45 and 90 mg at W24.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects who did not met EE criteria at W16 were crossed over to Ustekinumab 45 and 90 mg at W24.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the

arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects who did not met EE criteria at W16 were crossed over to Ustekinumab 45 and 90 mg at W24.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects who did not met EE criteria at W16 were crossed over to Ustekinumab 45 and 90 mg at W24.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects who did not met EE criteria at W16 were crossed over to Ustekinumab 45 and 90 mg at W24.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo subcutaneous (SC) injection at Weeks 0, 4, and 16. At Week (W) 16, subjects who met early escape (EE) criteria (less than [<] 10 percent [%] improvement from baseline in both total back pain and morning stiffness measures at both Week 12 and Week 16) were administered open-label golimumab 50 mg SC administrations at Week 16 and every 4 weeks (q4w) thereafter through Week 52. At Week 24 all subjects (with the exception of subjects who qualified for EE) were re-randomized to receive either ustekinumab 45 or 90 mg SC injection at Weeks 24 and 28 followed by every 12 weeks (q12w) dosing, with the last administration of study agent at Week 52.	
Reporting group title	Ustekinumab 45mg
Reporting group description:	
Subjects received ustekinumab 45 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects were to receive placebo SC injection to maintain the blind.	
Reporting group title	Ustekinumab 90mg
Reporting group description:	
Subjects received Ustekinumab 90 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, Subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects received placebo SC injection to maintain the blind.	

Reporting group values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg
Number of subjects	104	106	105
Title for AgeCategorical Units: subjects			
<65	101	103	102
>=65	3	3	3
Title for AgeContinuous Units: years			
arithmetic mean	40.8	41.4	41.5
standard deviation	± 11.72	± 11.33	± 11.02
Title for Gender Units: subjects			
Female	24	18	13
Male	80	88	92

Reporting group values	Total		
Number of subjects	315		
Title for AgeCategorical Units: subjects			
<65	306		
>=65	9		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	55		
Male	260		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo subcutaneous (SC) injection at Weeks 0, 4, and 16. At Week (W) 16, subjects who met early escape (EE) criteria (less than [<] 10 percent [%] improvement from baseline in both total back pain and morning stiffness measures at both Week 12 and Week 16) were administered open-label golimumab 50 mg SC administrations at Week 16 and every 4 weeks (q4w) thereafter through Week 52. At Week 24 all subjects (with the exception of subjects who qualified for EE) were re-randomized to receive either ustekinumab 45 or 90 mg SC injection at Weeks 24 and 28 followed by every 12 weeks (q12w) dosing, with the last administration of study agent at Week 52.

Reporting group title	Ustekinumab 45mg

Reporting group description:

Subjects received ustekinumab 45 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects were to receive placebo SC injection to maintain the blind.

Reporting group title	Ustekinumab 90mg

Reporting group description:

Subjects received Ustekinumab 90 mg SC injection at Weeks 0 and 4, followed by q12w dosing, with the last administration of study agent at Week 52. At Week 16, Subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24, subjects received placebo SC injection to maintain the blind.

Primary: Percentage of Subjects who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 Response at Week 24

End point title	Percentage of Subjects who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 Response at Week 24

End point description:

ASAS 40:Improvement from baseline of greater than or equal to (>=) 40% and with an absolute improvement from baseline of at least 2 on 0 to10cm scale in at least 3 of 4 domains: Patient's global assessment(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,10=impossible) of 10 questions,8 of relate to participant's functional anatomy,2 relate to participant's ability to cope with life), Inflammation(0 to 10cm;0=none,10=very severe);no worsening at all from baseline in remaining domain. Response is based on imputed data using treatment failure(TF)(consider non-responders at and after TF),EE rule(consider non-responder at W20,24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). FAS: subjects randomized and received at least one dose of study agent. Subjects analyzed based on randomized treatment group assigned, regardless of treatment received.

End point type	Primary

End point timeframe:

Week (W) 24

End point values	Placebo	Ustekinumab 45mg	Ustekinumab 90mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	73	67	
Units: Percentage of subjects				
number (not applicable)	12.3	19.2	26.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ustekinumab 45mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Percentage difference
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	18.6

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ustekinumab 90mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Percentage difference
Point estimate	14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	27.6

Secondary: Percentage of Subjects who Achieved an ASAS 20 Response at Week 24

End point title	Percentage of Subjects who Achieved an ASAS 20 Response at Week 24

End point description:

ASAS 20: Improvement from baseline of >= 20% from baseline and absolute improvement from baseline of 1 on a 0 to 10 cm scale in at least 3 of following 4 domains: Patient's global assessment (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 participant's functional anatomy and 2 relate to participant's ability to cope with life), Inflammation(0 to 10cm;0=none,10=very severe);absence of deterioration (>= 20% and worsening of at least 1 on 0 to 10cm scale) from baseline in remaining domain. Response based on imputed data using TF(consider non-responders at and after TF),EE rule(consider non-responder at W 20 and 24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). MFAS population was used. Subjects analyzed based on randomized treatment group assigned, regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)	27.4	31.5	37.3	

Statistical analyses

No statistical analyses for this end point

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

End point description:

BASDAI used to measure the AS disease severity. It consists of 6 questions: fatigue, spinal pain, arthralgia (joint pain) or swelling, enthesitis (inflammation of tendons and ligaments), morning stiffness(MS) (2 questions: duration and severity). Each question is an easy to answer 10 cm VAS, with 0 being none,10 being very severe and for last question related to MS duration: 0(0 hours[h]),10(2 or more hours). Order to give 5 symptoms equal weight, mean of 2 questions about MS added to total of remaining 4 scores, final BASDAI score(0-10) is average of overall total score. Higher BASDAI score indicates more severe AS symptom. 50% improvement in response based on imputed data using TF (consider non-responders at and after TF),EE rules(consider non-responder at W20.24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). Modified-FAS population was used. Subjects analyzed based on randomized treatment group assigned, regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)	11.0	15.1	28.4	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

BASFI is composed with 10 questions(question is answered with visual analogue scale 0-10 cm assess disease severity, first 8 questions regarding to functional anatomy related activities and 2 questions related to daily activities of AS. Each question is a10cm VAS value between 0 (easy) and 10 (impossible). The final BASFI score is the mean of 10 scores.BASFI score is average of 10 responses, min. value of 0 and max. value 10. Higher BASFI score shows more severe functional limitations due to AS. Missing data were imputed using early escape (consider non-responder at Wk 20,24). Modified-FAS population was used. Subjects analyzed based on randomized treatment group they were assigned to regardless of treatment received. Here 'N' signifies number of Subjects 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	44	44	42	
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.29 (± 2.219)	-1.74 (± 2.724)	-2.17 (± 2.438)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

ASDAS includes CRP mg/L;4 self-reported items:total back pain(TBP), duration of morning stiffness(DMS),peripheral pain (PP),patient global assessment (PGA).ASDAS scores (=0.121*TBP)+(0.110*PGA)+(0.073*PP)+(0.058*DMS)+(0.579*Ln(CRP+1).Disease activity,TBP,PP on numeric rating scale (0(normal)-10 (very severe) ,DMS (0 to 10, with 0 being none and 10 representing duration of =>2 hrs). Inactive disease defined as an ASDAS score <1.3. Missing data is imputed using treatment failure(consider non-responders at and after treatment failure),early escape rules(consider non-responder at Week 20 and 24), NRI(missing responses at post baseline visit imputed as non-responder). Modified-FAS population was used. Subjects analyzed based on randomized treatment group they were assigned to regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)	0	2.7	3.0	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change from baseline in hsCRP was reported. hsCRP is a sensitive laboratory assay for serum levels of C-Reactive Protein, which is a biomarker of inflammation. Early escape rule was applied (measurement value at Week 20 and Week 24 was set as missing). Modified-FAS population was used. Subjects analyzed based on randomized treatment group they were assigned to regardless of treatment received. Here 'n' signifies number of subjects analyzed for the 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	73	73	67	
Units: Milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Change at week 4 (n=71,69,67)	0.12 (± 2.211)	-0.35 (± 2.171)	-0.12 (± 1.604)	
Change at week 8 (n=69,68,65)	-0.18 (± 2.526)	-0.54 (± 2.213)	-0.24 (± 2.555)	
Change at week 12 (n=68,68,64)	-0.02 (± 2.836)	-0.36 (± 2.495)	0.05 (± 2.842)	
Change at week 16 (n=66,67,64)	-0.06 (± 2.676)	-0.21 (± 2.333)	0.12 (± 2.720)	
Change at week 20 (n=42,45,44)	0.23 (± 2.266)	-0.11 (± 1.611)	-0.40 (± 2.198)	
Change at week 24 (n=43,44,43)	-0.36 (± 2.067)	-0.14 (± 2.041)	-0.26 (± 1.850)	

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 include CRP mg/L;4 self-reported items:total back pain(TBP), duration of morning stiffness(DMS), peripheral pain (PP),patient global assessment (PGA).ASDAS scores (=0.121*TBP)+(0.110*PGA)+(0.073*PP)+(0.058*DMS)+(0.579*Ln(CRP+1).Disease activity,TBP,PP on numeric rating scale (0(normal)-10 (very severe) ,DMS (0 to 10, with 0 being none and 10 representing duration of =>2 hrs). Inactive disease defined as an ASDAS score <1.3. Missing data is imputed using treatment failure(consider non-responders at and after treatment failure),early escape rules(consider non-responder at Week 20 and 24), NRI(missing responses at post baseline visit imputed as non-responder). Modified-FAS population was used. Subjects analyzed based on randomized treatment group they were assigned to regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)				
Week 4	0	0	0	
Week 8	0	2.7	0	
Week 12	0	1.4	3.0	
Week 16	0	1.4	3.0	
Week 20	1.4	1.4	1.5	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

ASAS 40:Improvement from baseline of >=40% and with an absolute improvement from baseline of at least 2 on 0 to10cm scale in at least 3 of 4 domains: Patient's global assessment(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,10=impossible) of 10 questions,8 of relate to participant's functional anatomy,2 relate to participant's ability to cope with life), Inflammation(0 to 10cm;0=none,10=very severe);no worsening at all from baseline in remaining domain. Response is based on imputed data using treatment failure(TF)(consider non-responders at and after TF),EE rule(consider non-responder at W20,24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). FAS: subjects randomized and received at least one dose of study agent. Subjects analyzed

based on randomized treatment group assigned, regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)				
Week 4	6.8	8.2	11.9	
Week 8	11.0	12.3	16.4	
Week 12	6.8	15.1	19.4	
Week 16	9.6	15.1	20.9	
Week 20	12.3	21.9	25.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved ASAS 20 Responses at Week 4, 8, 12, 16 and 20

End point title	Percentage of Participants who Achieved ASAS 20 Responses at Week 4, 8, 12, 16 and 20

End point description:

ASAS 20: Improvement from baseline of >= 20% from baseline and absolute improvement from baseline of 1 on a 0 to 10 cm scale in at least 3 of following 4 domains: Patient's global assessment (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 participant's functional anatomy and 2 relate to participant's ability to cope with life), Inflammation(0 to 10cm;0=none,10=very severe);absence of deterioration (>= 20% and worsening of at least 1 on 0 to 10cm scale) from baseline in remaining domain. Response based on imputed data using TF(consider non-responders at and after TF),EE rule(consider non-responder at W 20 and 24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). MFAS population was used. Subjects analyzed based on randomized treatment group assigned, regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)				
Week 4	19.2	26.0	31.3	
Week 8	20.5	34.2	29.9	
Week 12	24.7	30.1	32.8	
Week 16	23.3	21.9	35.8	
Week 20	28.8	35.6	41.8	

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 used to measure the AS disease severity. It consists of 6 questions: fatigue, spinal pain, arthralgia (joint pain) or swelling, enthesitis (inflammation of tendons and ligaments), morning stiffness(MS) (2 questions: duration and severity). Each question is an easy to answer 10 cm VAS, with 0 being none,10 being very severe and for last question related to MS duration: 0(0 hours[h]),10(2 or more hours). Order to give 5 symptoms equal weight, mean of 2 questions about MS added to total of remaining 4 scores, final BASDAI score(0-10) is average of overall total score. Higher BASDAI score indicates more severe AS symptom. 50% improvement in response based on imputed data using TF (consider non-responders at and after TF),EE rules(consider non-responder at W20.24),non-responder[NRI] (missing responses at post baseline visit imputed as non-responder). Modified-FAS population was used. Subjects analyzed based on randomized treatment group assigned, regardless of 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	73	73	67	
Units: Percentage of subjects				
number (not applicable)				
Week 4	5.5	6.8	11.9	
Week 8	8.2	11.0	13.4	
Week 12	4.1	15.1	11.9	
Week 16	11.0	15.1	16.4	
Week 20	8.2	16.4	19.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in BASFI Total Score at Week 4, 8, 12, 16 and 20

End point title	Change From Baseline in BASFI Total Score at Week 4, 8, 12, 16 and 20

End point description:

BASFI composed with 10questions(question answered with visual analogue scale 0-10 cm assess disease severity, first 8 questions regarding to functional anatomy related activities and 2questions related to daily activities of AS. Each question is10cm VAS value between 0(easy) and10 (impossible). The final BASFI score is mean of 10 scores.BASFI score is average of 10 responses, min. value of 0 and max. value100. Higher BASFI score shows more severe functional limitations due to AS. Missing data were imputed using early escape (consider non-responder at Wk 20,24). Modified-FAS population was used. Subjects analyzed based on randomized treatment group they were assigned to regardless of treatment received. Here 'n' signifies number of subjects analyzed for this endpoint at specific timepoints.

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	73	73	67	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 4 (n=71,69,66)	-0.58 (± 1.571)	-0.69 (± 1.662)	-0.73 (± 1.915)	
Change at Week 8 (n=69,68,64)	-0.66 (± 2.099)	-0.86 (± 2.010)	-1.02 (± 2.010)	
Change at Week 12 (n=68,68,63)	-0.73 (± 2.406)	-0.70 (± 2.380)	-0.77 (± 2.459)	
Change at Week 16 (n=66,67,63)	-0.58 (± 2.053)	-0.54 (± 2.491)	-0.80 (± 2.574)	
Change at Week 20 (n=41,45,43)	-1.45 (± 2.353)	-1.73 (± 2.564)	-2.16 (± 2.140)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 64

Adverse event reporting additional description:

The safety analysis set included all subjects who received at least 1 (partial or complete) administration of study agent, i.e., the treated population. Adverse events were reported according to the treatment they actually received, regardless of the treatments they are randomized to.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo SC injection at Weeks 0, 4, and 16. At Week 16, subjects who met EE criteria were administered open-label golimumab 50 mg SC administrations at Week 16 and q4w thereafter through Week 52. At Week 24 all subjects (with the exception of subjects who qualified for EE) were re-randomized to receive either ustekinumab 45 or 90 mg SC injection at Weeks 24 and 28 followed by q12w dosing. Included all subjects, but adverse events for subjects who early escaped at Week 16 or crossed over at Week 24 are only counted up to Week 16 or Week 24 respectively.

Reporting group title	Placebo to Golimumab

Reporting group description:

Subjects randomized to placebo SC who met early escape criteria and received golimumab from Week 16; adverse events are counted from early escape onward.

Reporting group title	Placebo to Ustekinumab 45mg

Reporting group description:

Subjects randomized to placebo SC and then rerandomized to receive ustekinumab 45 mg at Week 24; adverse events are counted from crossover onward.

Reporting group title	Placebo to Ustekinumab 90mg

Reporting group description:

Subjects randomized to placebo SC and then re randomized to receive ustekinumab 90 mg at Week 24; adverse events are counted from crossover onward.

Reporting group title	Ustekinumab 45mg Only

Reporting group description:

Subjects received ustekinumab 45 mg SC injection at Weeks 0 and 4, followed by q12w dosing. Adverse events for subjects who early escaped at Week 16 are only counted up to Week 16.

Reporting group title	Ustekinumab 45mg to Golimumab

Reporting group description:

Subjects randomized to ustekinumab 45 mg SC who met early escape criteria and received golimumab from Week 16; adverse events are counted from early escape onward.

Reporting group title	Ustekinumab 90mg Only

Reporting group description:

Subjects received Ustekinumab 90 mg SC injection at Weeks 0 and 4, followed by q12w dosing. Adverse events for subjects who early escaped at Week 16 are only counted up to Week 16.

Reporting group title	Ustekinumab 90mg to Golimumab

Reporting group description:

Subjects randomized to ustekinumab 90 mg SC who met early escape criteria and received golimumab from Week 16; adverse events are counted from early escape onward.

Serious adverse events	Placebo	Placebo to Golimumab	Placebo to Ustekinumab 45mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 104 (0.96%)	2 / 21 (9.52%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial Ischaemia			
subjects affected / exposed	0 / 104 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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			
Iritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Nausea			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Vomiting			

subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine Polyp			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Uterine Prolapse			
subjects affected / exposed	1 / 104 (0.96%)	0 / 21 (0.00%)	0 / 21 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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 Amyloidosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Musculoskeletal and connective tissue disorders			
Axial Spondyloarthritis			

subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Back Pain			
subjects affected / exposed	0 / 104 (0.00%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (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	Placebo to Ustekinumab 90mg	Ustekinumab 45mg Only	Ustekinumab 45mg to Golimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	3 / 106 (2.83%)	1 / 21 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial Ischaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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			
Iritis			

subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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
Nausea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine Polyp			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Prolapse			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Amyloidosis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 106 (0.00%)	0 / 21 (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
Musculoskeletal and connective tissue disorders			
Axial Spondyloarthritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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
Back Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (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
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ustekinumab 90mg Only	Ustekinumab 90mg to Golimumab	

Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 105 (5.71%)	1 / 20 (5.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial Ischaemia			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	1 / 105 (0.95%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Iritis			
subjects affected / exposed	0 / 105 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine Polyp			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Prolapse			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Amyloidosis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (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	2 / 105 (1.90%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 105 (0.95%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 105 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Placebo to Golimumab	Placebo to Ustekinumab 45mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 104 (18.27%)	0 / 21 (0.00%)	2 / 21 (9.52%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	6 / 104 (5.77%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	9	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	5 / 104 (4.81%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	7	0	0
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Injection Site Bruising			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vitreous Haemorrhage			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 104 (4.81%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	5	0	0
Dyspepsia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Mouth Ulceration			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Skin Disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Spondylitis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 104 (1.92%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	1 / 104 (0.96%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 104 (3.85%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 104 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo to Ustekinumab 90mg	Ustekinumab 45mg Only	Ustekinumab 45mg to Golimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	19 / 106 (17.92%)	7 / 21 (33.33%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 106 (1.89%)	2 / 21 (9.52%)
occurrences (all)	1	2	2
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 106 (1.89%)	2 / 21 (9.52%)
occurrences (all)	1	2	2
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	4 / 106 (3.77%)	1 / 21 (4.76%)
occurrences (all)	0	5	1
General disorders and administration site conditions			
Injection Site Bruising			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vitreous Haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Mouth Ulceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Skin Disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Spondylitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 106 (0.94%)	0 / 21 (0.00%)
occurrences (all)	0	1	0

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 22 (0.00%)	2 / 106 (1.89%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Pharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	3 / 106 (2.83%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Viral Infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 106 (1.89%)	1 / 21 (4.76%)
occurrences (all)	0	2	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 22 (0.00%)	4 / 106 (3.77%)	2 / 21 (9.52%)
occurrences (all)	0	4	2
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 22 (0.00%)	0 / 106 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Ustekinumab 90mg Only	Ustekinumab 90mg to Golimumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 105 (17.14%)	10 / 20 (50.00%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	4 / 105 (3.81%)	2 / 20 (10.00%)	
occurrences (all)	4	2	
Aspartate Aminotransferase Increased			
subjects affected / exposed	3 / 105 (2.86%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	1 / 105 (0.95%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			

Neutropenia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1	1 / 20 (5.00%) 1	
General disorders and administration site conditions Injection Site Bruising subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	1 / 20 (5.00%) 3	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	1 / 20 (5.00%) 1	
Eye disorders Vitreous Haemorrhage subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	1 / 20 (5.00%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Mouth Ulceration subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0 0 / 105 (0.00%) 0 0 / 105 (0.00%) 0	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0	
Skin and subcutaneous tissue disorders Skin Disorder subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	1 / 20 (5.00%) 1	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1	1 / 20 (5.00%) 1	
Musculoskeletal and connective tissue disorders Spondylitis subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	1 / 20 (5.00%) 1	

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 105 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 105 (0.95%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Respiratory Tract Infection			
subjects affected / exposed	1 / 105 (0.95%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Viral Infection			
subjects affected / exposed	1 / 105 (0.95%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	8 / 105 (7.62%)	1 / 20 (5.00%)	
occurrences (all)	10	1	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 105 (0.95%)	1 / 20 (5.00%)	
occurrences (all)	1	1	

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
17 May 2017	The study was discontinued before it was fully enrolled due to lack of efficacy of either dose of ustekinumab 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.

Notes: