Clinical trial results:
A Phase 2, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Study Evaluating the Efficacy and Safety of Ustekinumab (STELARA ®) and CNTO 1959 Administered Subcutaneously in Subjects With Active Rheumatoid Arthritis Despite Concomitant Methotrexate Therapy

Summary

EudraCT number	2011-001122-18
Trial protocol	HU CZ BG
Global end of trial date	05 May 2014

Results information

Result version number	v1
This version publication date	06 July 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	CNTO1275ARA2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01645280
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg 30, 2340, Beerse, Belgium,
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, 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?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of ustekinumab and CNTO 1959 in reducing signs and symptoms of disease in subjects with active Rheumatoid Arthritis [RA] despite concomitant methotrexate (MTX) therapy, and to evaluate the safety of ustekinumab and CNTO 1959 in this population.

Protection of trial subjects:

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. Known instances of nonconformance were documented and are not considered to have had an impact on the overall conclusions of this study. The study protocol and amendment were reviewed by an Independent Ethics Committee (IEC) or Institutional Review Board (IRB). Safety assessments included monitoring and recording all adverse effects [AE] and serious adverse effects [SAE], laboratory evaluations (hematology, blood chemistry, urinalysis and immunogenicity), vital signs, body weight, electro cardio gram [ECG] and injection site reactions through Week 48.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	02 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 23
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Colombia: 43
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Poland: 35
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Ukraine: 46
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	273
EEA total number of subjects	64

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)	234
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 250 participants were planned, 274 were randomized, and 273 participants were treated.

Pre-assignment

Screening details:

Randomization was to be stratified by investigational site and by participant's C-reactive protein (CRP) level at screening. Based on inclusion criteria of participants with screening CRP greater than or equal to (>=) 0.80 milligram per deciliter [mg/dL], it was assumed that 60 percent (%) to 80% of participants had CRP >=1.50 (mg/dL) at screening.

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, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo+MTX

Arm description:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

Arm title	Ustekinumab+MTX 90 mg q8w

Arm description:

Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

Arm type	Experimental
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose).

Arm title	Ustekinumab+MTX 90 mg q12w

Arm description:

Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy

Arm type	Experimental

Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Weeks 0, 4, then every 12 weeks (Weeks 16 and 28) + MTX (pre-study dose)

Arm title	CNTO1959+MTX 50 mg q8w

Arm description:

CNTO1959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

Arm type	Experimental
Investigational medicinal product name	CNTO 1959
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

at Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28)+ MTX (pre-study dose)

Arm title	CNTO1959+MTX 200 mg q8w

Arm description:

CNTO1959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

Arm type	Experimental
Investigational medicinal product name	CNTO 1959
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

Number of subjects in period 1	Placebo+MTX	Ustekinumab+MTX 90 mg q8w	Ustekinumab+MTX 90 mg q12w
Started	55	54	55
Completed	50	51	50
Not completed	5	3	5
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	2	-	3
Other	1	-	-
Lack of efficacy	2	2	1

Number of subjects in period 1	CNTO1959+MTX 50 mg q8w	CNTO1959+MTX 200 mg q8w
Started	55	54
Completed	51	50
Not completed	4	4
Adverse event, serious fatal	-	-

Consent withdrawn by subject	1	-
Adverse event, non-fatal	2	-
Other	-	-
Lack of efficacy	1	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo+MTX
Reporting group description:	
At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)	
Reporting group title	Ustekinumab+MTX 90 mg q8w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	Ustekinumab+MTX 90 mg q12w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 50 mg q8w
Reporting group description:	
CNTO1959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 200 mg q8w
Reporting group description:	
CNTO1959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	

Reporting group values	Placebo+MTX	Ustekinumab+MTX 90 mg q8w	Ustekinumab+MTX 90 mg q12w
Number of subjects	55	54	55
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	51	46	44
From 65 to 84 years	4	8	11
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	51.1	50.7	51.4
standard deviation	± 10.57	± 13.13	± 13.59
Title for Gender Units: subjects			
Female	48	46	47
Male	7	8	8

Reporting group values	CNTO1959+MTX 50 mg q8w	CNTO1959+MTX 200 mg q8w	Total
Number of subjects	55	54	273
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	50	43	234
From 65 to 84 years	5	11	39
85 years and over	0	0	0

Title for AgeContinuous Units: years			
arithmetic mean	49.9	54.6	
standard deviation	± 12.85	± 11.34	-
Title for Gender Units: subjects			
Female	45	42	228
Male	10	12	45

End points

End points reporting groups

Reporting group title	Placebo+MTX
Reporting group description:	
At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)	
Reporting group title	Ustekinumab+MTX 90 mg q8w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	Ustekinumab+MTX 90 mg q12w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 50 mg q8w
Reporting group description:	
CNTO1959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 200 mg q8w
Reporting group description:	
CNTO1959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Subject analysis set title	Intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The intent-to-treat (ITT) population included all randomized participants. For early escape, data at or prior to Week 16 were carried forward through Week 28.	

Primary: Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 28

End point title	Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 28
End point description:	
The ACR 20 responders are participants with at least 20 percent (%) improvement from Baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: 1) patient's assessment of arthritis pain-visual analog scale, 2) patient's global assessment of disease activity-visual analog scale, 3) physician's global assessment of disease activity-visual analog scale, 4) patient’s assessment of physical function as measured by health assessment questionnaire-disability index (HAQ-Di), 5) C-reactive protein (CRP).	
End point type	Primary
End point timeframe:	
Week 28	

End point values	Placebo+MTX	Ustekinumab+ MTX 90 mg q8w	Ustekinumab+ MTX 90 mg q12w	CNTO1959+MTX 50 mg q8w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	54	55	55
Units: percentage of participants				
number (not applicable)	40	52.7	54.5	38.2

End point values	CNTO1959+MTX 200 mg q8w			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percentage of participants				
number (not applicable)	44.4			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.184
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 2
Comparison groups	Ustekinumab+MTX 90 mg q12w v Placebo+MTX
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.13
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo+MTX v CNTO1959+MTX 200 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.642
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo+MTX v CNTO1959+MTX 50 mg q8w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.832
Method	Cochran-Mantel-Haenszel

Secondary: Change From Baseline in Disease Activity Index Score 28 (DAS28; Using C-reactive Protein [CRP]) Score at Week 28

End point title	Change From Baseline in Disease Activity Index Score 28 (DAS28; Using C-reactive Protein [CRP]) Score at Week 28

End point description:

The DAS28 calculated from the number of swollen joints (SJC) and painful joints (PJC) using the 28 joints count, CRP milligram per liter (mG/L) and patient's global assessment (PGA) of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 <=3.2 = low disease activity, DAS28 >3.2 to 5.1 = moderate to high disease activity.

End point type	Secondary

End point timeframe:

From Baseline to Week 28

End point values	Placebo+MTX	Ustekinumab+ MTX 90 mg q8w	Ustekinumab+ MTX 90 mg q12w	CNTO1959+MTX 50 mg q8w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	54	55	55
Units: units on scale				
least squares mean (standard error)	-0.94 (± 0.174)	-1.52 (± 0.185)	-1.49 (± 0.183)	6.07 (± 0.821)

End point values	CNTO1959+MTX 200 mg q8w			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: units on scale				
least squares mean (standard error)	-1.21 (± 0.17)			

Statistical analyses

Statistical analysis title	Statistical analysis 5
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.019
Method	ANCOVA

Statistical analysis title	Statistical analysis 6
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q12w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.025
Method	ANCOVA

Statistical analysis title	Statistical analysis 7
Comparison groups	Placebo+MTX v CNTO1959+MTX 200 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.248
Method	ANCOVA

Statistical analysis title	Statistical analysis 8
Comparison groups	Placebo+MTX v CNTO1959+MTX 50 mg q8w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.045
Method	ANCOVA

Secondary: Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 12

End point title	Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 12

End point description:

The ACR 20 responders are participants with at least 20 percent (%) improvement from Baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: 1) Patient's Assessment of Arthritis Pain-Visual Analog Scale, 2) Patient's Global Assessment of Disease Activity-Visual Analog Scale, 3) Physician's Global Assessment of Disease Activity-Visual Analog Scale, 4) Patient’s Assessment of Physical Function as measured by Health Assessment Questionnaire-Disability Index (HAQ-DI), 5) C-reactive Protein (CRP).

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo+MTX	Ustekinumab+ MTX 90 mg q8w	Ustekinumab+ MTX 90 mg q12w	CNTO1959+MTX 50 mg q8w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	54	55	55
Units: percentage of participants				
number (not applicable)	29.1	37	34.5	20

End point values	CNTO1959+MTX 200 mg q8w			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percentage of participants				
number (not applicable)	33.3			

Statistical analyses

Statistical analysis title	Statistical analysis 9
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.381
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 10
Comparison groups	Ustekinumab+MTX 90 mg q12w v Placebo+MTX
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.543
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 11
Comparison groups	Placebo+MTX v CNTO1959+MTX 200 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.629
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 12
Comparison groups	Placebo+MTX v CNTO1959+MTX 50 mg q8w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.273
Method	Cochran-Mantel-Haenszel

Secondary: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 28

End point title	Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 28

End point description:

The Health Assessment Questionnaire-Disability Index (HAQ-DI): participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty.

End point type	Secondary

End point timeframe:

Baseline and Week 28

End point values	Placebo+MTX	Ustekinumab+ MTX 90 mg q8w	Ustekinumab+ MTX 90 mg q12w	CNTO1959+MTX 50 mg q8w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	54	55	55
Units: units on scale				
least squares mean (standard error)	-0.3 (± 0.074)	-0.48 (± 0.072)	-0.44 (± 0.071)	-0.39 (± 0.076)

End point values	CNTO1959+MTX 200 mg q8w			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: units on scale				
least squares mean (standard error)	-0.41 (± 0.075)			

Statistical analyses

Statistical analysis title	Statistical analysis 13
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.06
Method	ANCOVA

Statistical analysis title	Statistical analysis 14
Comparison groups	Placebo+MTX v Ustekinumab+MTX 90 mg q12w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.134
Method	ANCOVA

Statistical analysis title	Statistical analysis 15
Comparison groups	Placebo+MTX v CNTO1959+MTX 200 mg q8w
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.28
Method	ANCOVA

Statistical analysis title	Statistical analysis 16
Comparison groups	Placebo+MTX v CNTO1959+MTX 50 mg q8w
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.345
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0
Reporting groups	
Reporting group title	Placebo+MTX
Reporting group description:	
Placebo with Methotrexate concomitant therapy	
Reporting group title	Ustekinumab+MTX 90 mg q8w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	Ustekinumab+MTX 90 mg q12w
Reporting group description:	
Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 50 mg q8w
Reporting group description:	
CNTO1959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	
Reporting group title	CNTO1959+MTX 200 mg q8w
Reporting group description:	
CNTO1959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy	

Serious adverse events	Placebo+MTX	Ustekinumab+MTX 90 mg q8w	Ustekinumab+MTX 90 mg q12w
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 55 (7.27%)	4 / 54 (7.41%)	3 / 55 (5.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer Stage I			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Squamous Cell Carcinoma of Lung			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Concussion			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Vascular disorders			
Shock			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Angina Unstable			
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	0 / 55 (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
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Transient Ischaemic Attack			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
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			

Rheumatoid Arthritis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	0 / 55 (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
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Lobar Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CNTO1959+MTX 50 mg q8w	CNTO1959+MTX 200 mg q8w	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)	3 / 54 (5.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer Stage I			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma of Lung			

subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Shock			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Unstable			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (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			
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			

subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (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			
Rheumatoid Arthritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (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			
Appendicitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (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: 3 %

Non-serious adverse events	Placebo+MTX	Ustekinumab+MTX 90 mg q8w	Ustekinumab+MTX 90 mg q12w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 55 (32.73%)	20 / 54 (37.04%)	17 / 55 (30.91%)
Investigations			
Blood Creatine Phosphokinase Increased			

subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 55 (7.27%)	4 / 54 (7.41%)	2 / 55 (3.64%)
occurrences (all)	4	4	2
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 55 (5.45%)	2 / 54 (3.70%)	5 / 55 (9.09%)
occurrences (all)	5	3	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 55 (1.82%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 55 (1.82%)	2 / 54 (3.70%)	1 / 55 (1.82%)
occurrences (all)	1	2	1
Influenza Like Illness			
subjects affected / exposed	2 / 55 (3.64%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	2	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	2	1	1
Dyspepsia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			

Back Pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Rheumatoid Arthritis			
subjects affected / exposed	1 / 55 (1.82%)	2 / 54 (3.70%)	5 / 55 (9.09%)
occurrences (all)	1	2	7
Spinal Pain			
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	2 / 55 (3.64%)
occurrences (all)	2	1	2
Tendonitis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 55 (1.82%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	1	2	2
Influenza			
subjects affected / exposed	3 / 55 (5.45%)	1 / 54 (1.85%)	3 / 55 (5.45%)
occurrences (all)	4	2	3
Nasopharyngitis			
subjects affected / exposed	3 / 55 (5.45%)	5 / 54 (9.26%)	4 / 55 (7.27%)
occurrences (all)	4	8	6
Respiratory Tract Infection Viral			
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	2	0	2
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 55 (1.82%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	2	3	2

Non-serious adverse events	CNTO1959+MTX 50 mg q8w	CNTO1959+MTX 200 mg q8w	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 55 (25.45%)	21 / 54 (38.89%)	
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	

Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 55 (1.82%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 55 (3.64%)	3 / 54 (5.56%)	
occurrences (all)	2	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 55 (1.82%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Influenza Like Illness			
subjects affected / exposed	1 / 55 (1.82%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 55 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 54 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back Pain			

subjects affected / exposed	3 / 55 (5.45%)	1 / 54 (1.85%)	
occurrences (all)	4	1	
Rheumatoid Arthritis			
subjects affected / exposed	2 / 55 (3.64%)	4 / 54 (7.41%)	
occurrences (all)	2	4	
Spinal Pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 55 (3.64%)	4 / 54 (7.41%)	
occurrences (all)	2	5	
Influenza			
subjects affected / exposed	3 / 55 (5.45%)	3 / 54 (5.56%)	
occurrences (all)	3	4	
Nasopharyngitis			
subjects affected / exposed	3 / 55 (5.45%)	4 / 54 (7.41%)	
occurrences (all)	6	7	
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 55 (1.82%)	1 / 54 (1.85%)	
occurrences (all)	2	2	
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 55 (3.64%)	2 / 54 (3.70%)	
occurrences (all)	2	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2012	The length of study was reduced to a 28-week placebo-controlled period with 20-week follow-up period. The hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) testings were added at the screening. The total blood volume was updated to include the additional laboratory testing added to the protocol. The treatment failure criteria were updated to include all reasons for discontinuation of study agent (such as due to adverse events [AEs]). A 12-lead ECG was added to the Week 28 safety evaluations. Instructions were added to the protocol to avoid unblinding by the Principal Investigator because of serious adverse events (SAEs) related to disease progression. Added that ribonucleic acid (RNA) would be measured from whole blood as well as serum in the study. The unit 10-cm was removed in reference to Visual Analogue Scale (VAS) since an electronic patient-reported outcome e-PRO) device was to be used to collect the VAS in the study. Preplanned surgery/procedure(s) row was removed from the time and events schedule since this row did not pertain to this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

No notable study limitations were identified by the Sponsor.

Notes: