Clinical trial results:
A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Induction Therapy in Subjects with Moderately to Severely Active Crohn's Disease

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-022759-42
Trial protocol	DE GB BE ES NL HU IS BG IT
Global end of trial date	28 October 2014

Results information

Result version number	v1 (current)
This version publication date	25 May 2016
First version publication date	25 May 2016

Trial information

Trial identification

Sponsor protocol code	CNTO1275CRD3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01369342
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Janssen Research & Development, LLC , Clinical Registry Group, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen Research & Development, LLC , Clinical Registry Group, 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	28 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 August 2014
Global end of trial reached?	Yes
Global end of trial date	28 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the efficacy of Intravenous (IV) induction regimens of ustekinumab in inducing clinical response in subjects with moderately to severely active Crohn's disease who have demonstrated an inadequate response to or have failed to tolerate corticosteroids or immunomodulators: 6-mercaptopurine (6-MP), azathioprine (AZA), methotrexate (MTX), and to evaluate the safety of IV induction regimens of ustekinumab in subjects with moderately to severely active Crohn's disease.

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. Safety was evaluated based on Adverse events (AEs) and clinical laboratory test results (including hematology and serum chemistry), Physical examinations and 12 Lead Electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2011
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	Australia: 20
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Canada: 42
Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Hungary: 61
Country: Number of subjects enrolled	Iceland: 2
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Japan: 26

Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	New Zealand: 14
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Serbia: 15
Country: Number of subjects enrolled	United States: 220
Country: Number of subjects enrolled	South Africa: 33
Worldwide total number of subjects	640
EEA total number of subjects	213

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)	611
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at multiple sites in North America, South America, Eastern Europe, Western Europe, the Asia-Pacific region, and South Africa that evaluated ustekinumab in subjects with Crohn's disease.

Pre-assignment

Screening details:

A total of 640 subjects were randomized in the study. Out of which, 214 in the placebo group, 213 in the ustekinumab 130 milligram (mg) group, and 213 in the ustekinumab 6 milligram per kilogram (mg/kg) group.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

All subjects randomized to single Intravenous (IV) dose of placebo at Week 0.

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

Dosage and administration details:

All subjects were to receive single Intravenous (IV) dose of placebo at Week 0.

Arm title	Ustekinumab 130 milligram (mg)

Arm description:

Subjects randomized to 130 milligram of Ustekinumab given intravenously at week 0.

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

Dosage and administration details:

Subjects were to receive to 130 milligram of Ustekinumab given intravenously at week 0.

Arm title	Ustekinumab ~ 6 milligram per kilogram (mg/kg)

Arm description:

Subjects randomized to weight-range ustekinumab approximately (~) 6 mg/kg: 260 mg (weight less than or equal to (<=) 55 kg) 390 mg (weight more than (>) 55 kg and below or equivivalent to (<=) 85 kg) and 520 mg (weight more than (>) 85 kg).

Arm type	Experimental

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

Dosage and administration details:

Subjects were to receive Ustekinumab ~ 6 mg/kg administered intravenously at week 0.

Number of subjects in period 1	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Started	214	213	213
Completed	201	204	210
Not completed	13	9	3
Consent withdrawn by subject	7	7	2
Other	1	-	-
Lost to follow-up	5	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All subjects randomized to single Intravenous (IV) dose of placebo at Week 0.	
Reporting group title	Ustekinumab 130 milligram (mg)
Reporting group description:	
Subjects randomized to 130 milligram of Ustekinumab given intravenously at week 0.	
Reporting group title	Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Reporting group description:	
Subjects randomized to weight-range ustekinumab approximately (~) 6 mg/kg: 260 mg (weight less than or equal to (<=) 55 kg) 390 mg (weight more than (>) 55 kg and below or equivivalent to (<=) 85 kg) and 520 mg (weight more than (>) 85 kg).	

Reporting group values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Number of subjects	214	213	213
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	204	203	204
From 65 to 84 years	10	10	9
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	40.1	39.2	38.8
standard deviation	± 13.09	± 13.74	± 13.65
Title for Gender Units: subjects			
Female	113	107	122
Male	101	106	91

Reporting group values	Total		
Number of subjects	640		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	611		
From 65 to 84 years	29		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	342		
Male	298		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
All subjects randomized to single Intravenous (IV) dose of placebo at Week 0.	
Reporting group title	Ustekinumab 130 milligram (mg)
Reporting group description:	
Subjects randomized to 130 milligram of Ustekinumab given intravenously at week 0.	
Reporting group title	Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Reporting group description:	
Subjects randomized to weight-range ustekinumab approximately (~) 6 mg/kg: 260 mg (weight less than or equal to (<=) 55 kg) 390 mg (weight more than (>) 55 kg and below or equivivalent to (<=) 85 kg) and 520 mg (weight more than (>) 85 kg).	

Primary: Number of subjects in Clinical Response at week 6

End point title	Number of subjects in Clinical Response at week 6
End point description:	
Clinical response at Week 6 is defined as a reduction from baseline in the Crohn's Disease Activity Index (CDAI) score of at least (>=) 100 points. Subjects with a baseline CDAI score of 220 to 248 points were considered to be in clinical response if a CDAI score of less than (<) 150 was attained. Only subjects randomized after study re-start were included in the key efficacy analysis (please refer protocol amendment section).	
End point type	Primary
End point timeframe:	
Week 6	

End point values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	209	209	209	
Units: Number of Subjects	60	108	116	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The proportion of subjects was summarized and compared between each of ustekinumab treatment groups and placebo group using 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at significance level of 0.05. A fixed sequence testing procedure was used to control the Type I error at the 0.05 level over the primary and major secondary endpoints described herein.	
Comparison groups	Placebo v Ustekinumab ~ 6 milligram per kilogram (mg/kg)

Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab 130 milligram (mg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Secondary: Number of Subjects in Clinical Remission at week 8

End point title	Number of Subjects in Clinical Remission at week 8

End point description:

Clinical remission at Week 8 was defined as a Crohn's Disease Activity Index (CDAI) score of <150 points. Only subjects randomized after study re-start were included in the key efficacy analysis.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	209	209	209	
Units: Number of Subjects	41	64	84	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (<=300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab 130 milligram (mg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Cochran-Mantel-Haenszel chi-square test

Secondary: Number of Subjects in Clinical response at week 8

End point title	Number of Subjects in Clinical response at week 8

End point description:

Clinical response at Week 8 is defined as a reduction from baseline in the Crohn's Disease Activity Index (CDAI) score of more than or equal to (>=)100 points. Subjects with a baseline CDAI score of 220 to 248 points were considered to be in clinical response if a CDAI score of <150 was attained. Only subjects randomized after study re-start were included in the key efficacy analysis.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	209	209	209	
Units: Number of Subjects	67	99	121	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment

groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab 130 milligram (mg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Secondary: Number of Subjects in 70-point Response at Week 6

End point title	Number of Subjects in 70-point Response at Week 6

End point description:

The endpoint of 70-point response at Week 6 was defined as a reduction from baseline in the Crohn's Disease Activity Index (CDAI) score of more than or equal to (>=) 70 points at Week 6. Only subjects randomized after study re-start were included in the key efficacy analysis.

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	209	209	209	
Units: Number of Subjects	81	123	135	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab 130 milligram (mg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Secondary: Number of subjects in 70-point Response at Week 3

End point title	Number of subjects in 70-point Response at Week 3

End point description:

The endpoint of 70-point response at Week 3 was defined as a reduction from baseline in the Crohn’s Disease Activity Index (CDAI) score of more than or equal to (>=) 70 points at Week 3.Only subjects randomized after study re-start were included in the key efficacy analysis

End point type	Secondary

End point timeframe:

Week 3

End point values	Placebo	Ustekinumab 130 milligram (mg)	Ustekinumab ~ 6 milligram per kilogram (mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	209	209	209	
Units: Number of Subjects	66	103	106	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab ~ 6 milligram per kilogram (mg/kg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The proportion of subjects was summarized and compared between each of the ustekinumab treatment groups and the placebo group using a 2-sided Cochran-Mantel-Haenszel chi-square test, stratified by study region (Asia, Eastern Europe, or rest of world) and CDAI score (≤300 or >300), at a significance level of 0.05.

Comparison groups	Placebo v Ustekinumab 130 milligram (mg)
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel chi-square test

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to week 8	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All subjects received single Intravenous (IV) dose of placebo at Week 0.	
Reporting group title	Ustekinumab approximately (~) 6 mg/kg
Reporting group description:	
Subjects received weight-range ustekinumab ~ 6 mg/kg: 260 mg (weight less than or equal to (<=) 55 kg) 390 mg (weight more than (>) 55 kg and below or equivivalent to (<=) 85 kg) and 520 mg (weight more than (>) 85 kg).	
Reporting group title	Ustekinumab 130 mg
Reporting group description:	
Subjects received 130 milligram of Ustekinumab given intravenously at week 0.	

Serious adverse events	Placebo	Ustekinumab approximately (~) 6 mg/kg	Ustekinumab 130 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 212 (7.08%)	9 / 211 (4.27%)	10 / 216 (4.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Incisional Hernia			
subjects affected / exposed	0 / 212 (0.00%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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			
Headache			

subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 212 (0.00%)	1 / 211 (0.47%)	0 / 216 (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
Impaired Healing			
subjects affected / exposed	0 / 212 (0.00%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 212 (0.00%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 211 (0.47%)	0 / 216 (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
Crohn's Disease			
subjects affected / exposed	5 / 212 (2.36%)	2 / 211 (0.95%)	5 / 216 (2.31%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	0 / 212 (0.00%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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
Localised Intraabdominal Fluid Collection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 211 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	1 / 212 (0.47%)	2 / 211 (0.95%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Perforation			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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			
Bile Duct Stone			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax Spontaneous			

subjects affected / exposed	0 / 212 (0.00%)	1 / 211 (0.47%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Granuloma			
subjects affected / exposed	0 / 212 (0.00%)	1 / 211 (0.47%)	0 / 216 (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
Infections and infestations			
Anal Abscess			
subjects affected / exposed	3 / 212 (1.42%)	0 / 211 (0.00%)	2 / 216 (0.93%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 211 (0.47%)	0 / 216 (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
Genital Herpes			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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
Pneumonia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 211 (0.00%)	0 / 216 (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

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

Non-serious adverse events	Placebo	Ustekinumab approximately (~) 6 mg/kg	Ustekinumab 130 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 212 (20.75%)	44 / 211 (20.85%)	40 / 216 (18.52%)
Nervous system disorders			
Headache			

subjects affected / exposed	14 / 212 (6.60%)	10 / 211 (4.74%)	20 / 216 (9.26%)
occurrences (all)	17	16	26
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 212 (4.72%)	11 / 211 (5.21%)	6 / 216 (2.78%)
occurrences (all)	12	11	6
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 212 (2.36%)	11 / 211 (5.21%)	7 / 216 (3.24%)
occurrences (all)	5	12	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 212 (4.72%)	14 / 211 (6.64%)	10 / 216 (4.63%)
occurrences (all)	10	14	11
Upper Respiratory Tract Infection			
subjects affected / exposed	11 / 212 (5.19%)	7 / 211 (3.32%)	4 / 216 (1.85%)
occurrences (all)	12	7	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2011	The amendment includes the changes like; Sponsor temporarily suspended dosing of subjects with the proposed new formulation of ustekinumab in November 2011 because a stability issue was identified with the batch of the IV drug (130 milligram (mg) ustekinumab in 26 mL [5 milligram per milliliter (mg/mL)]) used in the study. To prevent significant delay to study CNTO1275CRD3002, the Sponsor substituted the new formulation (130 mg ustekinumab in 26 ml) with the approved 90 mg/mL ustekinumab formulation for the protocol-specified IV induction administrations. The 3 Phase 3 protocols were amended to incorporate the use of the 90 mg/mL formulation and the studies were completed, or are ongoing, with the 90 mg/mL formulation (supplied as 90 mg in 1 mL nominal volume and 45 mg in 0.5 mL nominal volume). Because knowledge of the stability issue could potentially bias the assessments, data from the 12 subjects who were randomized before the study was temporarily suspended were not used in the planned analyses. To maintain the originally planned sample size of 600 subjects, which was needed to power the primary endpoint analysis, the planned enrollment in the Statistical Analysis Plan (SAP) was prospectively changed to 612 (600+12) subjects
03 June 2014	The amendment included clarification on changes in the description of the prohibited medications and wording regarding the initiation or medication dosage change for Crohn's disease-specific medications; clarification that discussion with the medical monitor regarding the use of a local or central laboratory for selected tests was appropriate; removal of the requirement for the IVRS/IWRS system to project the expected number of subjects in the primary analysis population of the maintenance study and possibly increase enrollment for this induction study; clarification of the internal procedures for determining which SAEs were appropriate for reporting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 November 2011	The global study was interrupted due to issues with the clinical supply.	17 February 2012

Notes:

Limitations and caveats

None reported