Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, an Anti-TNF Monoclonal Antibody, Administered Intravenously, in Subjects with Active Ankylosing Spondylitis

Summary

EudraCT number	2014-000241-74
Trial protocol	DE
Global end of trial date	14 October 2016

Results information

Result version number	v1 (current)
This version publication date	27 October 2017
First version publication date	27 October 2017

Trial information

Trial identification

Sponsor protocol code	CNTO148AKS3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02186873
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Biologics, BV
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333CM
Public contact	Clinical Registry Group, Janssen Biologics, BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Biologics, BV, 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	11 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of intravenous (IV) administration of golimumab 2 milligram per kilogram (mg/kg) in subjects with active ankylosing spondylitis (AS) by assessing the reduction in signs and symptoms of AS.

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 evaluations included measurement of vital signs, assessment of AEs, physical examinations, electrocardiograms (screening only), concomitant medications, infusion reaction evaluations, and assessments of allergic reactions. Tuberculosis (TB) evaluations were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2014
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	Canada: 2
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Poland: 68
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Ukraine: 59
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	208
EEA total number of subjects	76

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)	207
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 312 subjects screened, 208 subjects were randomized (105 to golimumab 2 milligram per kilogram [mg/kg] and 103 to placebo group) and treated.

Period 1

Period 1 title	Overall Period (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	Group 1: Placebo then Golimumab

Arm description:

Subjects received placebo intravenous (IV) infusions at Weeks 0, 4, and 12. At Week 16 subjects were crossed over to golimumab and received IV golimumab 2 milligram per kilogram (mg/kg) infusion at Weeks 16, 20, and every 8 weeks (q8w) thereafter through Week 52.

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

Dosage and administration details:

Subjects received placebo intravenous infusions at Weeks 0, 4, and 12.

Investigational medicinal product name	Golimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received golimumab 2 mg/kg infusion at Weeks 16, 20, and every 8 weeks (q8w) thereafter through Week 52.

Arm title	Group 2: Golimumab

Arm description:

Subjects received IV golimumab 2 mg/kg infusion at Weeks 0, 4 and then q8w thereafter through Week 52. Subjects received a placebo infusion at Week 16 to maintain the treatment blind.

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

Dosage and administration details:

Subjects received intravenous golimumab 2 mg/kg infusion at Weeks 0, 4 and q8w thereafter through Week 52.

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

Dosage and administration details:

Subjects received placebo intravenous (IV) infusions at Week 16.

Number of subjects in period 1	Group 1: Placebo then Golimumab	Group 2: Golimumab
Started	103	105
End of Control Period	99	105
Completed	94	97
Not completed	9	8
Consent withdrawn by subject	7	2
Adverse event, non-fatal	1	3
Lost to follow-up	1	2
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Placebo then Golimumab
Reporting group description:	
Subjects received placebo intravenous (IV) infusions at Weeks 0, 4, and 12. At Week 16 subjects were crossed over to golimumab and received IV golimumab 2 milligram per kilogram (mg/kg) infusion at Weeks 16, 20, and every 8 weeks (q8w) thereafter through Week 52.	
Reporting group title	Group 2: Golimumab
Reporting group description:	
Subjects received IV golimumab 2 mg/kg infusion at Weeks 0, 4 and then q8w thereafter through Week 52. Subjects received a placebo infusion at Week 16 to maintain the treatment blind.	

Reporting group values	Group 1: Placebo then Golimumab	Group 2: Golimumab	Total
Number of subjects	103	105	208
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	102	105	207
From 65 to 84 years	1	0	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	39.2	38.4	
standard deviation	± 10.75	± 10.11	-
Title for Gender Units: subjects			
Female	26	19	45
Male	77	86	163

End points

End points reporting groups

Reporting group title	Group 1: Placebo then Golimumab

Reporting group description:

Subjects received placebo intravenous (IV) infusions at Weeks 0, 4, and 12. At Week 16 subjects were crossed over to golimumab and received IV golimumab 2 milligram per kilogram (mg/kg) infusion at Weeks 16, 20, and every 8 weeks (q8w) thereafter through Week 52.

Reporting group title	Group 2: Golimumab

Reporting group description:

Subjects received IV golimumab 2 mg/kg infusion at Weeks 0, 4 and then q8w thereafter through Week 52. Subjects received a placebo infusion at Week 16 to maintain the treatment blind.

Primary: Percentage of Subjects Who Achieved at Least 20 Percent Improvement From Baseline in the Assessment of SpondyloArthritis International Society (ASAS 20) at Week 16

End point title	Percentage of Subjects Who Achieved at Least 20 Percent Improvement From Baseline in the Assessment of SpondyloArthritis International Society (ASAS 20) at Week 16

End point description:

ASAS 20 defined as 20 percent (%) improvement compared to baseline in the ASAS Working Group criteria: that is, greater than or equal to (>=)20% improvement from baseline in at least 3 of the 4 domains: patient's global assessment of disease activity (0=very well,10 =very poor), total back pain (0=no pain,10=most severe pain), function (self-assessment using BASFI [0=no functional impairment to 10= maximal impairment]), inflammation (0=none,10=very severe) with an absolute improvement of at least 1 (0-10 centimeter (cm) visual analogue scale [VAS]), and an absence of deterioration (defined as >=20% worsening and absolute worsening of at least 1 on a 0-10 cm scale) in the potential remaining domain. Full Analysis Set (FAS) included all subjects who were randomized in the study.

End point type	Primary

End point timeframe:

Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	105		
Units: Percentage of Subjects				
number (not applicable)	26.2	73.3		

Statistical analyses

Statistical analysis title	Statistics Analysis 1
Comparison groups	Group 2: Golimumab v Group 1: Placebo then Golimumab

Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percent Difference
Point estimate	47.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.18
upper limit	58.99

Secondary: Percentage of Subjects Who Achieved at Least 40 Percent Improvement From Baseline in the Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16

End point title	Percentage of Subjects Who Achieved at Least 40 Percent Improvement From Baseline in the Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16

End point description:

An ASAS 40 response is defined as >=40% improvement from baseline in 3 of 4 domains: patient's global assessment of disease activity (0=very well, 10=very poor), total back pain (0=no pain, 10=most severe pain), function (self-assessment using BASFI (0=no functional impairment to 10=maximal impairment), inflammation (0=none, 10=very severe) with an absolute improvement of at least 2 (0-10 cm VAS), and no deterioration in the remaining domain. FAS included all subjects who were randomized in the study.

End point type	Secondary

End point timeframe:

Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	105		
Units: Percentage of Subjects				
number (not applicable)	8.7	47.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved at Least 50 Percent Improvement From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 16

End point title	Percentage of Subjects Who Achieved at Least 50 Percent Improvement From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 16

End point description:

The BASDAI is a self-assessment tool to determine disease activity using a VAS of 0-10 cm (0=none and 10=very severe) subject's answered 6 questions measuring fatigue, spinal pain, joint pain, enthesitis, and morning stiffness. The final BASDAI is calculated as a mean of individual questions with a final score range of 0 to 10 cm; 0=best and 10=worst. FAS included all subjects who were randomized in the study.

End point type	Secondary

End point timeframe:

Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	105		
Units: Percentage of Subjects				
number (not applicable)	14.6	41.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Score at Week 16

End point title	Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Score at Week 16

End point description:

The BASFI is a subject's self-assessment of physical function represented as a mean of 10 questions, each question rated on VAS 0 to 10 cm (VAS 0 to 10 cm; 0=easy to 10=impossible), 8 of which relate to the subject's functional anatomy and 2 of which relate to a participant's ability to cope with everyday life. FAS included all subjects who were randomized in the study. Here, 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	105		
Units: Units on a Scale				
arithmetic mean (standard deviation)	-0.471 (± 1.9558)	-2.386 (± 2.1300)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) Score at Week 16

End point title	Change From Baseline in Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) Score at Week 16

End point description:

The Medical Outcome Study health measure SF-36 questionnaire is a well-validated and widely used quality-of-life instrument. It is a self-administered survey that consists of 8 multi-item scales: The 4 subscales of the SF-36 comprises the PCS score (physical functioning, role-physical, bodily pain, and general health) and the 4 subscales of the SF-36 comprises the MCS score (vitality, social functioning, role-emotional, and mental health). PCS and MCS are scored from 0 to 100 with higher scores indicating better health (worst value is 0 and best value is 100), which are scored using a norm-based system where linear transformations are performed to transform scores to a mean of 50 and standard deviation of 10. FAS included all subjects who were randomized in the study. Here, 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: Units on Scale				
arithmetic mean (standard deviation)	2.86 (± 6.177)	8.52 (± 7.535)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form-36 Health Survey (SF-36) Mental Component Summary (MCS) Score at Week 16

End point title	Change From Baseline in Short Form-36 Health Survey (SF-36) Mental Component Summary (MCS) Score at Week 16

End point description:

The Medical Outcome Study health measure SF-36 questionnaire is a well-validated and widely used quality-of-life instrument. It is a self-administered survey that consists of 8 multi-item scales: The 4 subscales of the SF-36 comprises the PCS score (physical functioning, role-physical, bodily pain, and general health) and the 4 subscales of the SF-36 comprises the MCS score(vitality, social functioning, role-emotional, and mental health). PCS and MCS are scored from 0 to 100 with higher scores indicating better health (worst value is 0 and best value is 100), which are scored using a norm-based system where linear transformations are performed to transform scores to a mean of 50 and standard deviation of 10. FAS included all subjects who were randomized in the study. Here, 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: Units on Scale				
arithmetic mean (standard deviation)	0.78 (± 10.004)	6.47 (± 9.122)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Low Level of Disease Activity (ASAS Partial Remission) at Week 16

End point title	Percentage of Subjects With Low Level of Disease Activity (ASAS Partial Remission) at Week 16

End point description:

Low level of disease activity was measured by criteria for ASAS partial remission, defined as a value below 2 on a scale of 0 to 10 cm in each of the 4 ASAS domains: patient's global assessment of disease activity, total back pain, function (BASFI), inflammation. FAS included all subjects who were randomized in the study.

End point type	Secondary

End point timeframe:

Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	105		
Units: Percentage of Subjects				
number (not applicable)	3.9	16.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) at Week 16

End point title	Change From Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) at Week 16

End point description:

The ASQoL is a self-administered health-related quality of life (HRQOL) instrument. It consists of 18 items requesting a Yes or No response to questions related to the impact of the disease/condition (including pain) on sleep, mood, motivation, ability to cope, activities of daily living, independence, relationships, and social life. A score of 1 is given to a response of "yes" on each item and all item scores are summed to a total score with a range of 0 to 18. Higher scores indicate worse HRQOL. FAS included all subjects who were randomized in the study. Here, 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: Units on Scale				
arithmetic mean (standard deviation)	-1.8 (± 4.57)	-5.4 (± 5.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) at Week 16

End point title	Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) at Week 16

End point description:

The BASMI is an accurate and reproducible metrology index developed to assess the clinical changes in spinal movements of ankylosing spondylitis (AS) subjects. This index consists of 5 clinical measurements, including lumber side flexion, tragus to wall, lumbar flexion (modified Schober's), intermalleoar distance and cervical rotation. A BASMI response is represented as an aggregate score of 5 components (ranging from 0 [least impairment] to 10 [most impairment]). FAS included all subjects who were randomized in the study. Here, 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group 1: Placebo then Golimumab	Group 2: Golimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	100		
Units: Units on Scale				
arithmetic mean (standard deviation)	-0.10 (± 0.539)	-0.38 (± 0.625)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 weeks

Adverse event reporting additional description:

Safety Analysis set included all subjects who received at least 1 dose of study drug. Subjects who received placebo and crossed over to golimumab were included in placebo then golimumab 2 mg/kg arm and who received at least 1 dose of golimumab were included in placebo then golimumab 2 mg/kg and golimumab 2 mg/kg arms for safety analysis.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects who received placebo only (at least 1 dose) through Week 16. Follow-up was based on the period the subject was receiving placebo (from Week 0) up to the first golimumab 2 mg/kg dose for this treatment group.

Reporting group title	Placebo then Golimumab 2 mg/kg

Reporting group description:

Subjects who received placebo were crossed over to golimumab 2 mg/kg at Week 16. Subjects may have also inadvertently received golimumab 2 mg/kg prior to Week 16. Subjects may have missed one or more golimumab doses. Follow-up started from the first golimumab 2 mg/kg dose for this treatment group. Subjects who inadvertently received golimumab 2 mg/kg prior to Week 16 were applicable to include in this group.

Reporting group title	Golimumab 2 mg/kg

Reporting group description:

Subjects who received at least one dose of 2 mg/kg golimumab from Week 0 onward. Follow-up started from the first golimumab 2 mg/kg dose for this treatment group.

Serious adverse events	Placebo	Placebo then Golimumab 2 mg/kg	Golimumab 2 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 103 (0.00%)	1 / 99 (1.01%)	6 / 105 (5.71%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 103 (0.00%)	1 / 99 (1.01%)	0 / 105 (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
Cardiac disorders			
Sinus tachycardia			

subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
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			
Pancreatitis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Henoch-Schonlein purpura			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 99 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
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	Placebo then Golimumab 2 mg/kg	Golimumab 2 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 103 (2.91%)	16 / 99 (16.16%)	32 / 105 (30.48%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 103 (0.00%)	5 / 99 (5.05%)	7 / 105 (6.67%)
occurrences (all)	0	5	7
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 103 (0.97%)	1 / 99 (1.01%)	6 / 105 (5.71%)
occurrences (all)	1	1	10
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 103 (0.97%)	7 / 99 (7.07%)	17 / 105 (16.19%)
occurrences (all)	1	7	19
Upper respiratory tract infection			
subjects affected / exposed	1 / 103 (0.97%)	3 / 99 (3.03%)	12 / 105 (11.43%)
occurrences (all)	1	3	14

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? No

Limitations and caveats

None reported