Clinical trial results:
SIMPONI® to Arrest -cell Loss in Type 1 Diabetes

Summary

EudraCT number	2021-000189-13
Trial protocol	Outside EU/EEA
Global end of trial date	26 June 2020

Results information

Result version number	v1 (current)
This version publication date	14 July 2021
First version publication date	14 July 2021

Trial information

Trial identification

Sponsor protocol code	CNTO148DML2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02846545
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development, LLC
Sponsor organisation address	920, US Highway, Route 202, South Raritan, United States, 08869
Public contact	Clinical Registry Group, Janssen Research and Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research and 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to determine if golimumab could preserve beta-cell function in children and young adults with newly diagnosed Type 1 Diabetes (T1D).

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 Monitoring and evaluation of participants in this study focused on study agent, device-related, and disease-related safety issues. Monitoring included physical examinations (PEs), clinical laboratory tests, vital signs, concomitant medications, and adverse events (AEs) including injection site reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2016
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	United States: 84
Worldwide total number of subjects	84
EEA total number of subjects	0

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)	28
Adolescents (12-17 years)	40
Adults (18-64 years)	16
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 84 subjects with newly diagnosed T1D were enrolled. Of these, 56 subjects were randomized to the golimumab treatment arm and 28 subjects to the placebo treatment arm.

Period 1

Period 1 title	Double-blind Period: Week 0-52
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (Week 0-52)

Arm description:

Subjects received a subcutaneous (SC) injection of placebo every 2 weeks (q2w) through Week 52 to match the active arm.

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

Dosage and administration details:

Subjects received SC injection of placebo q2w through Week 52 to match the active arm.

Arm title	Golimumab (Week 0-52)

Arm description:

Subjects weighing less than (<) 45 kg received an induction dose of golimumab 60 milligrams/ meter square (mg/m^2) SC at Weeks 0 and 2 followed by a maintenance dose of 30 mg/m^2 SC at Week 4 and q2w through Week 52. Subjects weighing >=45 kg received an induction dose of golimumab 100 mg SC at Weeks 0 and 2 followed by a maintenance dose of golimumab 50 mg SC at Week 4 and q2w through Week 52.

Arm type	Experimental
Investigational medicinal product name	Golimumab
Investigational medicinal product code	
Other name	SIMPONI
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects weighing <45 kg received an induction dose of golimumab 60 mg/m^2 SC at Weeks 0 and 2 followed by a maintenance dose of 30 mg/m^2 SC at Week 4 and q2w through Week 52. Subjects weighing >=45 kg received an induction dose of golimumab 100 mg SC at Weeks 0 and 2 followed by a maintenance dose of golimumab 50 mg SC at Week 4 and q2w through Week 52.

Number of subjects in period 1	Placebo (Week 0-52)	Golimumab (Week 0-52)
Started	28	56
Completed	25	50
Not completed	3	6
Consent withdrawn by subject	1	5
Non-compliance with study drug	1	-
Lost to follow-up	1	1

Period 2

Period 2 title	Off-therapy Follow-up Period:Week 52-104
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (Week 52-104)

Arm description:

Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Golimumab (Week 52-104)

Arm description:

Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[1]	Placebo (Week 52-104)	Golimumab (Week 52-104)
Started	25	49
Completed	23	47
Not completed	2	2
Unspecified	1	1
Lost to follow-up	1	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 subject from the golimumab treatment group terminated study participation on the day

of the Week 52 visit.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (Week 0-52)
Reporting group description:	
Subjects received a subcutaneous (SC) injection of placebo every 2 weeks (q2w) through Week 52 to match the active arm.	
Reporting group title	Golimumab (Week 0-52)
Reporting group description:	
Subjects weighing less than (<) 45 kg received an induction dose of golimumab 60 milligrams/ meter square (mg/m^2) SC at Weeks 0 and 2 followed by a maintenance dose of 30 mg/m^2 SC at Week 4 and q2w through Week 52. Subjects weighing >=45 kg received an induction dose of golimumab 100 mg SC at Weeks 0 and 2 followed by a maintenance dose of golimumab 50 mg SC at Week 4 and q2w through Week 52.	

Reporting group values	Placebo (Week 0-52)	Golimumab (Week 0-52)	Total
Number of subjects	28	56	84
Title for AgeCategorical Units: subjects			
Children (2-11 years)	8	20	28
Adolescents (12-17 years)	13	27	40
Adults (18-64 years)	7	9	16
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	13.5	13.3	
standard deviation	± 4.01	± 3.73	-
Title for Gender Units: subjects			
Female	10	25	35
Male	18	31	49

End points

End points reporting groups

Reporting group title	Placebo (Week 0-52)
Reporting group description:	
Subjects received a subcutaneous (SC) injection of placebo every 2 weeks (q2w) through Week 52 to match the active arm.	
Reporting group title	Golimumab (Week 0-52)
Reporting group description:	
Subjects weighing less than (<) 45 kg received an induction dose of golimumab 60 milligrams/ meter square (mg/m^2) SC at Weeks 0 and 2 followed by a maintenance dose of 30 mg/m^2 SC at Week 4 and q2w through Week 52. Subjects weighing >=45 kg received an induction dose of golimumab 100 mg SC at Weeks 0 and 2 followed by a maintenance dose of golimumab 50 mg SC at Week 4 and q2w through Week 52.	
Reporting group title	Placebo (Week 52-104)
Reporting group description:	
Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.	
Reporting group title	Golimumab (Week 52-104)
Reporting group description:	
Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.	

Primary: Double-blind Period: C-peptide Area Under the Curve (AUC) Calculated From a 4 Hour Mixed Meal Tolerance Test (MMTT) at Week 52

End point title	Double-blind Period: C-peptide Area Under the Curve (AUC) Calculated From a 4 Hour Mixed Meal Tolerance Test (MMTT) at Week 52[1]
End point description:	
MMTT-Stimulated 4-Hour C-peptide AUC was defined as the mean area under the C-peptide level time curve over the 4-hour period divided by the duration after a mixed-meal tolerance test. Full Analysis Set (FAS) included all randomized subjects who took at least one dose (complete or partial) of study agent. Here 'N' (number of subjects analyzed) included all subjects who were evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	50		
Units: picomoles per millilitre (pmol/mL)				
arithmetic mean (standard deviation)	0.43 (± 0.388)	0.64 (± 0.423)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Change From Baseline in Insulin use in Units per Kilogram Body Weight per day

End point title	Double-blind Period: Change From Baseline in Insulin use in Units per Kilogram Body Weight per day

End point description:

Change from baseline in daily insulin use at Week 52 was reported. FAS included all randomized subjects who took at least one dose (complete or partial) of study agent.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: units/kilogram/day				
least squares mean (standard error)	0.243 (± 0.0419)	0.066 (± 0.0267)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (Week 0-52) v Golimumab (Week 0-52)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Mixed models analysis
Parameter estimate	Least Square (LS) Mean
Point estimate	-0.178
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	-0.08

Secondary: Double-blind Period: Change From Baseline in Glycosylated Haemoglobin (HbA1c) at Week 52

End point title	Double-blind Period: Change From Baseline in Glycosylated Haemoglobin (HbA1c) at Week 52

End point description:

Change from baseline in glycosylated HbA1c at Week 52 was reported. FAS included all randomized subjects who take at least one dose (complete or partial) of study agent.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: HbA1C %				
least squares mean (standard error)	0.56 (± 0.294)	0.47 (± 0.210)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (Week 0-52) v Golimumab (Week 0-52)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.802
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	0.63

Secondary: Double-blind Period: Hypoglycemic Event Rates

End point title	Double-blind Period: Hypoglycemic Event Rates

End point description:

A hypoglycemic event is defined as either a biochemically confirmed hypoglycemic episode or a severe hypoglycemic
event. Hypoglycemic event rates (defined as blood glucose (BG) levels of greater than equal to (<=) 70, 55, and 35 milligrams/deciliter (mg/dL) or clinical sequelae in the absence of a BG reading) up to Week 52. FAS which had all randomized subjects who took at least one dose (complete or partial) of study agent.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: events per year				
number (not applicable)	43.36	39.01		

Statistical analyses

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Hypoglycemia rate was analyzed by using a Poisson regression model with the number of hypoglycemia events through Week 52 as the response, treatment and gender as fixed factors, age and baseline HbA1c as covariates, and the duration of study participation through week 52 in logarithm as an offset variable.

Comparison groups	Placebo (Week 0-52) v Golimumab (Week 0-52)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0036
Method	Poisson regression model
Parameter estimate	Ratio of hypoglycemia rates
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.838
upper limit	0.966

Secondary: Double-blind Period: C-peptide Area Under the Curve (AUC) Calculated From a 4 Hour Mixed Meal Tolerance Test (MMTT) Over Time

End point title	Double-blind Period: C-peptide Area Under the Curve (AUC) Calculated From a 4 Hour Mixed Meal Tolerance Test (MMTT) Over Time

End point description:

MMTT-Stimulated 4-Hour C-peptide AUC is the mean area under the C-peptide level-time curve over the 4-hour period divided by the duration after a mixed-meal tolerance test. Full Analysis Set (FAS) included all randomized subjects who took at least one dose (complete or partial) of study agent. Here 'n' (number analyzed) included all subjects who were analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 26, 38, and 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: pmol/mL				
arithmetic mean (standard deviation)				
Baseline (n=28,56)	0.88 (± 0.634)	0.78 (± 0.396)		
Week 12 (n=26,52)	0.62 (± 0.426)	0.78 (± 0.355)		
Week 26 (n=25,49)	0.55 (± 0.424)	0.76 (± 0.380)		
Week 38 (n=24,49)	0.53 (± 0.423)	0.73 (± 0.424)		
Week 52 (n=25,50)	0.43 (± 0.388)	0.64 (± 0.423)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) as a Measure of Safety and Tolerability

End point title	Double-blind Period: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) as a Measure of Safety and Tolerability

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in clinical study subject administered medicinal product. It could be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to that medicinal product. Treatment emergent AEs were defined as AEs with onset during the treatment phase or that are a consequence of a pre-existing condition that has worsened since baseline.The safety analysis set included all randomized subjects who received at least 1 (partial or complete) dose of study agent, that is, the treated population.

End point type	Secondary

End point timeframe:

Up to Week 52 and Week 104

End point values	Placebo (Week 0-52)	Placebo (Week 52-104)	Golimumab (Week 0-52)	Golimumab (Week 52-104)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	25	56	49
Units: subjects	23	19	51	38

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Number of Subjects With Severe Adverse Events

End point title	Double-blind Period: Number of Subjects With Severe Adverse Events

End point description:

An AE was defined as any untoward medical occurrence in clinical study subject administered medicinal product. It could be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to that medicinal product. A SAE was defined as any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a suspected transmission of any infectious treatment via medicinal product and was medically important. The safety analysis set included all randomized subjects who received at least 1 (partial or complete) dose of study agent, that is, the treated population.

End point type	Secondary

End point timeframe:

Through Week 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Percentage of Participants With Severe Infections Through Week 52 and Week 104

End point title	Double-blind Period: Percentage of Participants With Severe Infections Through Week 52 and Week 104

End point description:

Subjects having 1 or more severe infections were evaluated and reported. The safety analysis set included all randomized subjects who received at least 1 (partial or complete) dose of study agent, that is, the treated population.

End point type	Secondary

End point timeframe:

Up to Week 52 and Week 104

End point values	Placebo (Week 0-52)	Placebo (Week 52-104)	Golimumab (Week 0-52)	Golimumab (Week 52-104)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	25	56	49
Units: percentage of subjects				
number (not applicable)	60.7	52.0	71.4	34.7

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Percentage of Participants With Study Agent Injection Site Reactions Up to Week 52

End point title	Double-blind Period: Percentage of Participants With Study Agent Injection Site Reactions Up to Week 52

End point description:

Percentage of participants with study agent injection site reactions up to Week 52 was reported. The safety analysis set included all randomized subjects who received at least 1 (partial or complete) dose of study agent, that is, the treated population.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo (Week 0-52)	Golimumab (Week 0-52)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	56		
Units: percentage of subjects				
number (not applicable)	28.6	23.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Serum Golimumab Concentrations

End point title	Double-blind Period: Serum Golimumab Concentrations[2]

End point description:

Serum samples were collected for the measurement of golimumab concentrations. PK Analysis Set included all subjects who received at least 1 golimumab injection and had sufficient PK samples for analysis. Here 'n' (number analyzed) included all subjects who were analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Preinjection: Week 0, Week 2, Week 4, Week 8, Week 12, and Week 26; Week 33, Week 38 (preinjection), Week 45 and Week 52 (preinjection)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	Golimumab (Week 0-52)			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: micrograms per millilitre (mcg/mL)				
arithmetic mean (standard deviation)				
Week 0 (n=56)	0.00 (± 0.000)			
Week 2 (n=56)	4.64 (± 1.506)			

Week 4 (n=56)	6.85 (± 2.168)			
Week 8 (n=54)	4.67 (± 1.930)			
Week 12 (n=52)	3.74 (± 2.032)			
Week 26 (n=50)	3.37 (± 2.011)			
Week 33 (n=49)	4.41 (± 2.825)			
Week 38 (n=50)	3.06 (± 2.127)			
Week 45 (n=49)	4.44 (± 2.828)			
Week 52 (n=49)	2.89 (± 2.022)			

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Number of Subjects with Antibodies to Golimumab

End point title	Double-blind Period: Number of Subjects with Antibodies to Golimumab[3]

End point description:

Number of subjects with antibodies to golimumab were reported. Population analyzed included all subjects with appropriate samples (had 1 or more samples) obtained after their first study agent administration.

End point type	Secondary

End point timeframe:

Up to Week 52

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	Golimumab (Week 0-52)			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: subjects	30			

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Period: Titers of Antibodies to Golimumab

End point title	Double-blind Period: Titers of Antibodies to Golimumab[4]

End point description:

Titers of antibodies to golimumab were evaluated. Population analyzed included all the subjects who were antibody positive, the peak titers for them were evaluated. Here '99999' is used as a placeholder because the data was not analyzed for this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 52

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	Golimumab (Week 0-52)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titers				
median (standard deviation)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 104

Adverse event reporting additional description:

The safety analysis set included all randomized subjects who received at least 1 (partial or complete) dose of study agent.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo (Week 0 - 52)

Reporting group description:

Subjects received a subcutaneous (SC) injection of placebo every 2 weeks (q2w) through Week 52 to match the active arm.

Reporting group title	Golimumab (Week 0 - 52)

Reporting group description:

Subjects weighing less than (<) 45 kg received an induction dose of golimumab 60 mg/m^2 SC at Weeks 0 and 2 followed by a maintenance dose of 30 mg/m2 SC at Week 4 and q2w through Week 52. Subjects weighing >=45 kg received an induction dose of golimumab 100 mg SC at Weeks 0 and 2 followed by a maintenance dose of golimumab 50 mg SC at Week 4 and q2w through Week 52.

Reporting group title	Placebo (Week 52 - 104)

Reporting group description:

Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.

Reporting group title	Golimumab (Week 52 - 104)

Reporting group description:

Following the 52-week double-blind period, subjects were monitored for an additional 52 weeks for safety.

Serious adverse events	Placebo (Week 0 - 52)	Golimumab (Week 0 - 52)	Placebo (Week 52 - 104)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	1 / 56 (1.79%)	1 / 25 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 56 (1.79%)	0 / 25 (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
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 28 (3.57%)	0 / 56 (0.00%)	0 / 25 (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
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 56 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Golimumab (Week 52 - 104)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 49 (8.16%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (Week 0 - 52)	Golimumab (Week 0 - 52)	Placebo (Week 52 - 104)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 28 (75.00%)	45 / 56 (80.36%)	14 / 25 (56.00%)

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	1	3	0
Injection Site Erythema			
subjects affected / exposed	3 / 28 (10.71%)	9 / 56 (16.07%)	0 / 25 (0.00%)
occurrences (all)	4	36	0
Injection Site Pain			
subjects affected / exposed	2 / 28 (7.14%)	6 / 56 (10.71%)	0 / 25 (0.00%)
occurrences (all)	2	11	0
Injection Site Swelling			
subjects affected / exposed	0 / 28 (0.00%)	4 / 56 (7.14%)	0 / 25 (0.00%)
occurrences (all)	0	14	0
Injection Site Urticaria			
subjects affected / exposed	3 / 28 (10.71%)	2 / 56 (3.57%)	0 / 25 (0.00%)
occurrences (all)	13	4	0
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)	4 / 56 (7.14%)	0 / 25 (0.00%)
occurrences (all)	1	5	0
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 28 (0.00%)	6 / 56 (10.71%)	1 / 25 (4.00%)
occurrences (all)	0	6	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 28 (28.57%)	9 / 56 (16.07%)	1 / 25 (4.00%)
occurrences (all)	10	10	1
Dyspnoea			
subjects affected / exposed	2 / 28 (7.14%)	0 / 56 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Nasal Congestion			
subjects affected / exposed	4 / 28 (14.29%)	5 / 56 (8.93%)	1 / 25 (4.00%)
occurrences (all)	6	9	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 28 (3.57%)	8 / 56 (14.29%)	0 / 25 (0.00%)
occurrences (all)	1	8	0

Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	0	3	0
Investigations			
Glycosylated Haemoglobin Increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 56 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 56 (0.00%)	0 / 25 (0.00%)
occurrences (all)	4	0	0
Limb Injury			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 28 (10.71%)	11 / 56 (19.64%)	1 / 25 (4.00%)
occurrences (all)	4	27	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 28 (7.14%)	2 / 56 (3.57%)	0 / 25 (0.00%)
occurrences (all)	2	2	0
Neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	0	3	0
Abdominal Pain Upper			
subjects affected / exposed	3 / 28 (10.71%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	3	3	0
Diarrhoea			
subjects affected / exposed	1 / 28 (3.57%)	5 / 56 (8.93%)	0 / 25 (0.00%)
occurrences (all)	1	5	0
Nausea			

subjects affected / exposed	2 / 28 (7.14%)	5 / 56 (8.93%)	1 / 25 (4.00%)
occurrences (all)	2	7	1
Vomiting			
subjects affected / exposed	2 / 28 (7.14%)	5 / 56 (8.93%)	0 / 25 (0.00%)
occurrences (all)	2	5	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 28 (7.14%)	1 / 56 (1.79%)	1 / 25 (4.00%)
occurrences (all)	2	1	1
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	0	4	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	3 / 56 (5.36%)	1 / 25 (4.00%)
occurrences (all)	0	3	1
Ear Infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 56 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Gastroenteritis			
subjects affected / exposed	2 / 28 (7.14%)	5 / 56 (8.93%)	0 / 25 (0.00%)
occurrences (all)	2	6	0
Influenza			
subjects affected / exposed	2 / 28 (7.14%)	6 / 56 (10.71%)	2 / 25 (8.00%)
occurrences (all)	2	6	2
Nasopharyngitis			
subjects affected / exposed	5 / 28 (17.86%)	10 / 56 (17.86%)	3 / 25 (12.00%)
occurrences (all)	8	16	4
Otitis Media			
subjects affected / exposed	2 / 28 (7.14%)	0 / 56 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Pharyngitis Streptococcal			
subjects affected / exposed	2 / 28 (7.14%)	3 / 56 (5.36%)	0 / 25 (0.00%)
occurrences (all)	2	4	0
Sinusitis			

subjects affected / exposed	2 / 28 (7.14%)	4 / 56 (7.14%)	0 / 25 (0.00%)
occurrences (all)	2	5	0
Upper Respiratory Tract Infection			
subjects affected / exposed	9 / 28 (32.14%)	17 / 56 (30.36%)	4 / 25 (16.00%)
occurrences (all)	11	31	4
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	2 / 28 (7.14%)	14 / 56 (25.00%)	2 / 25 (8.00%)
occurrences (all)	63	104	90

Non-serious adverse events	Golimumab (Week 52 - 104)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 49 (53.06%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Injection Site Erythema			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Injection Site Pain			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Injection Site Swelling			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Injection Site Urticaria			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Investigations			
Glycosylated Haemoglobin Increased			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Limb Injury			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Neutropenia			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Abdominal Pain Upper			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Ear Infection			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		

Influenza subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 5		
Otitis Media subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0		
Pharyngitis Streptococcal subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Sinusitis subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	8 / 49 (16.33%) 9		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	9 / 49 (18.37%) 141		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2016	The overall reason for the amendment was to incorporate feedback from health authorities into the protocol.
09 May 2017	The overall reason for the amendment was to update testing parameters, to address clarifications needed for severe hypoglycemia definition and to correct inconsistencies within the protocol.
27 August 2019	Subsequent to the granting of a single subject investigational new drug for a subject who had shown an increase in C-peptide at Week 52 and who had an insulin dose adjusted HbA1c (IDAA1c) score less than 9, the Data Monitoring Committee had recommended to re start active treatment for other subjects showing a similar response profile.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported