



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 | CNT0148DML2001 |
|-----------------------|----------------|

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/m²) 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.

| | |
|--|--|
| 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/m² 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.

| 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/m²) 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 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

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 (\pm 0.0419) | 0.066 (\pm 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 (\geq) 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/m² 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 occurrences (all) | 0 / 28 (0.00%) 0 | 3 / 56 (5.36%) 3 | 0 / 25 (0.00%) 0 |
| Investigations Glycosylated Haemoglobin Increased subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 56 (0.00%) 0 | 0 / 25 (0.00%) 0 |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Limb Injury subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 4 0 / 28 (0.00%) 0 | 0 / 56 (0.00%) 0 3 / 56 (5.36%) 3 | 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 4 | 11 / 56 (19.64%) 27 | 1 / 25 (4.00%) 1 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 0 / 28 (0.00%) 0 | 2 / 56 (3.57%) 2 3 / 56 (5.36%) 4 | 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 |
| Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) Abdominal Pain Upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea | 0 / 28 (0.00%) 0 3 / 28 (10.71%) 3 1 / 28 (3.57%) 1 | 3 / 56 (5.36%) 3 3 / 56 (5.36%) 3 5 / 56 (8.93%) 5 | 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 |

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

| | | | |
|---|-----------------------|-------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 4 / 56 (7.14%) 5 | 0 / 25 (0.00%) 0 |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 9 / 28 (32.14%) 11 | 17 / 56 (30.36%) 31 | 4 / 25 (16.00%) 4 |
| Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 63 | 14 / 56 (25.00%) 104 | 2 / 25 (8.00%) 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 occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Injection Site Erythema subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Injection Site Pain subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Injection Site Swelling subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Injection Site Urticaria subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | | |
| Immune system disorders Seasonal Allergy subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 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 occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | | |
| Nausea | | | |
| subjects affected / exposed occurrences (all) | 3 / 49 (6.12%) 3 | | |
| Vomiting | | | |
| subjects affected / exposed occurrences (all) | 4 / 49 (8.16%) 5 | | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in Extremity | | | |
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | | |
| Ear Infection | | | |
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | | |

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