# EU Clinical Trials Register

## Clinical trial results:

## Lean Efficacy Phase IIa Proof of concept trial (LEAAP). A multi-centre, double-blind, placebo controlled, randomised study in overweight and obese patients during twenty-six weeks, investigating the effect of EMP16-02 on body weight, safety and clinical biomarkers

### Summary

| | |
|---|---|
| EudraCT number | 2019-004545-32 |
| Trial protocol | SE |
| Global end of trial date | 30 August 2021 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 08 September 2022 |
| First version publication date | 08 September 2022 |

### Trial information

#### Trial identification

| | |
|---|---|
| Sponsor protocol code | EP-002 |

#### Additional study identifiers

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

Notes:

#### Sponsors

| | |
|---|---|
| Sponsor organisation name | Empros Pharma AB |
| Sponsor organisation address | Nanna Svartz väg 4, Solna, Sweden, SE-171 65 |
| Public contact | Arvid Söderhäll, Empros Pharma AB, +46 707233363, arvid.soderhall@emprospharma.com |
| Scientific contact | Arvid Söderhäll, Empros Pharma AB, +46 707233363, arvid.soderhall@emprospharma.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 | 30 August 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 August 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 August 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of the study drug EMP16-02 (120 mg orlistat [O]/40 mg acarbose [A]) on relative body weight loss after a 26-week period of oral treatment as compared to placebo.

Protection of trial subjects:

The ICFs included information that the data that were recorded, collected and processed could be transferred to the European Economic Area (EEA) or non-EEA countries. In accordance with the General Data protection Regulation (GDPR) (EU) 2016/679, the data did not allow for identification of any persons taking part in the study.

The potential study patient was informed that by signing the ICF he/she approved that authorized representatives from the Sponsor and CTC, the concerned Ethical Committee (EC) and CA had direct access to his/her medical records for verification of clinical study procedures. This agreement was substantiated in a separate document, according to local requirements.

The patient had the right to request access to his/her personal data and the right to request rectification of any data that were not correct and/or complete.

The Investigator had to file a Patient Identification List which included sufficient information to link records, i.e. the eCRF and clinical records. This list will be preserved for possible future inspections/audits but will not be made available to the Sponsor except for monitoring or auditing purposes.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 07 May 2020 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Scientific research |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Sweden: 156 |
| Worldwide total number of subjects | 156 |
| EEA total number of subjects | 156 |

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) | 135 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

# Subject disposition

## Recruitment

Recruitment details:

The subjects were recruited from CTC's database of healthy volunteers and patients, and from advertising in media (including social media).

## Pre-assignment

Screening details:

A total of 209 patients were screened and 156 were randomized (52 patients per treatment group). Thirty-seven patients were screening failures, 6 withdrew consent prior to randomization and 10 were not randomized due to other reasons (fulfilled eligibility criteria but were not needed in the study).

## Period 1

| | |
|---|---|
| Period 1 title | Main study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

This was a double-blind study, and the allocation of treatments was not disclosed until clean file had been declared and the database had been locked. Active treatment and placebo capsules were identical in appearance.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | EMP16-02 - 120/40 |

Arm description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02 -120/40 (120 mg orlistat/40 mg acarbose).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | EMP16-02 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

The drug product, EMP16-02, is a fixed dose combination (FDC) that contains 2 active pharmaceutical ingredients (APIs), namely orlistat (O) and acarbose (A). The IMP was supplied as oral modified release (MR) capsules in 2 different strengths: 60 mg O/20 mg A and 90 mg O/30 mg A. The dose used in this treatment arm was 120 mg O/40 mg A (2 capsules EMP16-02-60/20).

The IMP was to be taken halfway into a meal 3 times daily (TID) with approximately 100-200 mL water or other drink. The IMP was not to be taken on an empty stomach. The patients were recommended to leave 3-4 h between each meal/IMP dose.

The patients started with a titration period of 6 weeks during which the dose was sequentially increased in order to let patients gradually adapt to the acarbose dose. The IMP was administered TID also during the titration period. At week 7, all patients had reached their final intended dose and a 20-week treatment and observation period started.

| | |
|---|---|
| **Arm title** | EMP16-02 - 150/50 |

Arm description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02-150/50 (150 mg orlistat/50 mg acarbose).

| | |
|---|---|
| Arm type | Experimental |

| Investigational medicinal product name | EMP16-02 |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

The drug product, EMP16-02, is a fixed dose combination (FDC) that contains 2 active pharmaceutical ingredients (APIs), namely orlistat (O) and acarbose (A). The IMP was supplied as oral modified release (MR) capsules in 2 different strengths: 60 mg O/20 mg A and 90 mg O/30 mg A. The dose used in this treatment arm was 150 mg O/50 mg A (1 capsule EMP16-02-90/30 and 1 capsule EMP16-02-60/20).

The IMP was to be taken halfway into a meal 3 times daily (TID) with approximately 100-200 mL water or other drink. The IMP was not to be taken on an empty stomach. The patients were recommended to leave 3-4 h between each meal/IMP dose.

The patients started with a titration period of 6 weeks during which the dose was sequentially increased in order to let patients gradually adapt to the acarbose dose. The IMP was administered TID also during the titration period. At week 7, all patients had reached their final intended dose and a 20-week treatment and observation period started.

| **Arm title** | Placebo |
|---|---|

Arm description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive placebo.

| Arm type | Placebo |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo was a matching, oral capsule containing only cellulose.

The IMP was to be taken halfway into a meal 3 times daily (TID) for 26 weeks, together with approximately 100-200 mL water or other drink. The IMP was not to be taken on an empty stomach. The patients were recommended to leave 3-4 h between each meal/IMP dose.

| **Number of subjects in period 1** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo |
|---|---|---|---|
| Started | 52 | 52 | 52 |
| Completed | 44 | 45 | 46 |
| Not completed | 8 | 7 | 6 |
|     Consent withdrawn by subject | 3 | 2 | 5 |
|     Adverse event, non-fatal | 4 | 5 | - |
|     Lost to follow-up | 1 | - | - |
|     Protocol deviation | - | - | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | EMP16-02 - 120/40 |
|---|---|
| Reporting group description: | |

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02 -120/40 (120 mg orlistat/40 mg acarbose).

| Reporting group title | EMP16-02 - 150/50 |
|---|---|
| Reporting group description: | |

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02-150/50 (150 mg orlistat/50 mg acarbose).

| Reporting group title | Placebo |
|---|---|
| Reporting group description: | |

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive placebo.

| Reporting group values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo |
|---|---|---|---|
| Number of subjects | 52 | 52 | 52 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 49.4 | 50.7 | 49.5 |
| standard deviation | ± 12.2 | ± 13.6 | ± 12.8 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 38 | 36 | 37 |
| Male | 14 | 16 | 15 |
| Body Mass Index (BMI) | | | |
| Units: (kg/m2) | | | |
| arithmetic mean | 35.1 | 34.6 | 36.2 |
| standard deviation | ± 3.3 | ± 3.6 | ± 4.5 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 156 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |

| | | | |
|---|---|---|---|
| Preterm newborn infants (gestational age < 37 wks) | 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) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 111 | | |
| Male | 45 | | |
| Body Mass Index (BMI)<br>Units: (kg/m2) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| Reporting group title | EMP16-02 - 120/40 |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02 -120/40 (120 mg orlistat/40 mg acarbose).

| Reporting group title | EMP16-02 - 150/50 |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02-150/50 (150 mg orlistat/50 mg acarbose).

| Reporting group title | Placebo |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive placebo.

### Primary: Relative (%) change from baseline in body weight after 26 weeks

| End point title | Relative (%) change from baseline in body weight after 26 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. This end-point reports the mean relative (%) change from baseline (Visit 2, pre-dose) in body weight at Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Primary |
|---|---|

End point timeframe:

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (week 26), pre-dose | -5.8 (± 5.3) | -6.5 (± 4.4) | -0.7 (± 3.7) | |

### Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

Relative (%) change from baseline in body weight after 26 weeks of treatment with EMP16-02 (120 mg O/40 mg A) as compared to placebo was analysed using analysis of variance with treatment as the

independent variable. Hypothesis testing was two-sided. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [1] |
| Method | ANOVA |

Notes:

[1] - Hypothesis testing used a 5% significance level (α=0.05).

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

Relative (%) change from baseline in body weight after 26 weeks of treatment with EMP16-02 (150 mg O/50 mg A) as compared to placebo was analysed using analysis of variance with treatment as the independent variable. Hypothesis testing was two-sided. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

## Secondary: Absolute change from baseline in body weight after 14 and 26 weeks

| End point title | Absolute change from baseline in body weight after 14 and 26 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. This end-point reports the mean absolute change from baseline (Visit 2, pre-dose) in body weight at Week 14 and Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45[2] | 47[3] | 49[4] | |
| Units: kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -4.29 (± 3.19) | -4.83 (± 3.11) | -1.18 (± 3.30) | |
| Visit 5 (week 26), pre-dose | -5.75 (± 5.35) | -6.44 (± 4.59) | -0.78 (± 3.75) | |

Notes:

[2] - n=45 for Visit 4 and n=44 for Visit 5

[3] - n=47 for visit 4 and n=45 for Visit 5

[4] - n=49 for Visit 4 and n=46 for Visit 5

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 & Week 26 |
|---|---|

Statistical analysis description:

Absolute change from baseline in body weight was analysed using the ANCOVA model, with treatment as independent variable and weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 for Week 14 and 90 for Week 26.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [5] |
| Method | ANCOVA |

Notes:

[5] - This p-value applies for both Week 14 and Week 26.

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 & Week 26 |
|---|---|

Statistical analysis description:

Absolute change from baseline in body weight was analysed using the ANCOVA model, with treatment as independent variable and weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 for Week 14 and 91 for Week 26.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [6] |
| Method | ANCOVA |

Notes:

[6] - This p-value applies for both Week 14 and Week 26.

## Secondary: Relative (%) change from baseline in body weight after 14 weeks

| End point title | Relative (%) change from baseline in body weight after 14 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. This end-point reports the mean relative (%) change from baseline (Visit 2, pre-dose) at Week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7) and Visit 4 (Week 14).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (Week 14), pre-dose | -4.4 (± 3.1) | -4.8 (± 2.9) | -1.1 (± 3.1) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

Relative (%) change from baseline in body weight after 14 weeks of treatment with EMP16-02 (120 mg O/40 mg A) as compared to placebo was analysed using analysis of variance with treatment as the independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | Placebo v EMP16-02 - 120/40 |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

Relative (%) change from baseline in body weight after 14 weeks of treatment with EMP16-02 (150 mg O/50 mg A) as compared to placebo was analysed using analysis of variance with treatment as the independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

## Secondary: Proportion of patients with ≥5% and ≥10% decrease in body weight compared to baseline after 14 weeks

| End point title | Proportion of patients with ≥5% and ≥10% decrease in body weight compared to baseline after 14 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. This end-point reports the proportions (%) of patients with ≥5% and ≥10%

decrease in body weight relative to baseline (Visit 2, pre-dose) at Week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7) and Visit 4 (Week 14). | |

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| ≥5% decrease - Visit 4 (week 14), pre-dose | 31 | 43 | 14 | |
| ≥10% decrease - Visit 4 (week 14), pre-dose | 8.9 | 4.3 | 0 | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02-120/40 VS placebo - ≥5% decrease -Week 14 |
|---|---|
| Statistical analysis description: | |
| The proportion of patients with ≥5% decrease in body weight compared to baseline after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0504 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02-150/50 VS placebo - ≥5% decrease -Week 14 |
|---|---|
| Statistical analysis description: | |
| The proportion of patients with ≥5% decrease in body weight compared to baseline after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0021 |
| Method | Chi-squared |

| Statistical analysis title | EMP16-02-120/40 VS placebo- ≥10% decrease -Week 14 |
|---|---|

Statistical analysis description:

The proportion of patients with ≥10% decrease in body weight compared to baseline after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using chi-square test without continuity correction.

| Comparison groups | Placebo v EMP16-02 - 120/40 |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0329 |
| Method | Chi-squared |

| Statistical analysis title | EMP16-02-150/50 VS placebo- ≥10% decrease -Week 14 |
|---|---|

Statistical analysis description:

The proportion of patients with ≥10% decrease in body weight compared to baseline after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using chi-square test without continuity correction.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1445 |
| Method | Chi-squared |

## Secondary: Proportion of patients with ≥5% and ≥10% decrease in body weight compared to baseline after 26 weeks

| End point title | Proportion of patients with ≥5% and ≥10% decrease in body weight compared to baseline after 26 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. This end-point reports the proportions (%) of patients with ≥5% and ≥10% decrease in body weight relative to baseline (Visit 2, pre-dose) at Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| ≥5% decrease - Visit 5 (week 26), pre-dose | 55 | 67 | 13 | |
| ≥10% decrease - Visit 5 (week 26), pre-dose | 23 | 22 | 2.2 | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02-120/40 VS placebo - ≥5% decrease -Week 26 |
|---|---|
| Statistical analysis description: | |
| The proportion of patients with ≥5% decrease in body weight compared to baseline after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02-150/50 VS placebo - ≥5% decrease -Week 26 |
|---|---|
| Statistical analysis description: | |
| The proportion of patients with ≥5% decrease in body weight compared to baseline after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02-120/40 VS placebo- ≥10% decrease -Week 26 |
|---|---|
| Statistical analysis description: | |
| The proportion of patients with ≥10% decrease in body weight compared to baseline after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0029 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02-150/50 VS placebo- ≥10% decrease -Week 26 |
|---|---|

Statistical analysis description:

The proportion of patients with ≥10% decrease in body weight compared to baseline after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using chi-square test without continuity correction.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0034 |
| Method | Chi-squared |

## Secondary: Relative (%) change from baseline in BMI after 14 and 26 weeks

| End point title | Relative (%) change from baseline in BMI after 14 and 26 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. Height was measured in cm (no decimals) without shoes at screening (Visit 1). BMI was calculated based on the height measured at Visit 1 and the weight measured at each visit analyzed.

This end-point reports the mean relative (%) change in BMI from baseline (Visit 2, pre-dose) at Week 14 and Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26). Height was measured at Visit 1 Screening.

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45[7] | 47[8] | 49[9] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -4.4 (± 3.1) | -4.8 (± 3.0) | -1.0 (± 3.1) | |
| Visit 5 (Week 26), pre-dose | -5.8 (± 5.3) | -6.5 (± 4.4) | -0.7 (± 3.7) | |

Notes:

[7] - n=45 for Visit 4 and n=44 for Visit 5

[8] - n=47 for Visit 4 and n=45 for Visit 5

[9] - n=49 for Visit 4 and n=46 for Visit 5

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 & Week 26 |
|---|---|

Statistical analysis description:

The relative change from baseline in BMI after 14 and 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 and 90 for weeks 14 and 26 respectively.

| Comparison groups | Placebo v EMP16-02 - 120/40 |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [10] |
| Method | ANOVA |

Notes:

[10] - This p-value applies to both Week 14 and Week 26.

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 & Week 26 |
|---|---|

Statistical analysis description:

The relative change from baseline in BMI after 14 and 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 and 91 for weeks 14 and 26 respectively.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [11] |
| Method | ANOVA |

Notes:

[11] - This p-value applies to both Week 14 and Week 26.

## Secondary: Absolute change from baseline in BMI after 14 and 26 weeks

| End point title | Absolute change from baseline in BMI after 14 and 26 weeks |
|---|---|

End point description:

Weight was measured in kg (one decimal) without shoes and without thick clothes such as jumpers at pre-specified visits. Height was measured in cm (no decimals) without shoes at screening (Visit 1). BMI was calculated based on the height measured at Visit 1 and the weight measured at each visit analyzed.

This end-point reports the mean absolute change in BMI from baseline (Visit 2, pre-dose) at Week 14 and Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|
| End point timeframe: | |

Weight was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26). Height was measured at Visit 1 Screening.

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45[12] | 47[13] | 49[14] | |
| Units: kg/m2 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -1.55 (± 1.18) | -1.67 (± 1.08) | -0.40 (± 1.17) | |
| Visit 5 (Week 26), pre-dose | -2.08 (± 1.99) | -2.23 (± 1.57) | -0.25 (± 1.33) | |

Notes:

[12] - n=45 for Visit 4 and n=44 for Visit 5

[13] - n=47 for Visit 4 and n=45 for Visit 5

[14] - n=49 for Visit 4 and n=46 for Visit 5

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 & 26 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in BMI after 14 and 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subject included in the analyses were 94 and 90 for Week 14 and Week 26 respectively.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [15] |
| Method | ANCOVA |

Notes:

[15] - This p-value applies to both Week 14 and 26.

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 & 26 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in BMI after 14 and 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subject included in the analyses were 96 and 91 for Week 14 and Week 26 respectively.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|

| Number of subjects included in analysis | 96 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [16] |
| Method | ANCOVA |

Notes:

[16] - This p-value applies to both Week 14 and 26.

**Secondary: Absolute change from baseline in waist circumference after 14 weeks**

| End point title | Absolute change from baseline in waist circumference after 14 weeks |
|---|---|

End point description:

Waist circumference was measured in cm (one decimal) at pre-specified visits. Thi end-point reports the mean absolute change from baseline (Visit 2, Day 1) in waist circumference at Week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Waist circumference was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7) and Visit 4 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 46 | 48 | |
| Units: centimetre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -3.92 (± 6.02) | -3.83 (± 4.11) | -3.22 (± 4.67) | |

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in waist circumference after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5054 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in waist circumference after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5552 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in waist circumference after 26 weeks

| End point title | Absolute change from baseline in waist circumference after 26 weeks |
|---|---|

End point description:

Waist circumference was measured in cm (one decimal) at pre-specified visits. This end-point reports the mean absolute change from baseline (Visit 2, Day 1) in waist circumference at Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Waist circumference was assessed at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26) .

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 44 | 45 | |
| Units: centimetre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (Week 26), pre-dose | -6.61 (± 5.67) | -6.80 (± 5.52) | -3.36 (± 5.36) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in waist circumference after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0087 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in waist circumference after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0047 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in sagittal diameter after 14 weeks

| End point title | Absolute change from baseline in sagittal diameter after 14 weeks |
|---|---|

End point description:

Sagittal diameter was measured in cm (one decimal) at pre-specified visits. For measurement of the sagittal diameter, the patient lied down on his/her back while having knees bent, so that the lower back was in contact with the surface he/she was lying on. The distance from the back to the highest point of the abdomen was measured in cm while the patient exhaled.

This end-point reports the mean absolute change from baseline (Visit 2, Day 1) in sagittal diameter at week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Sagittal abdominal diameter was assessed at Visit 2 (Day 1) and Visit 4 (Week 14).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: centimetre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -1.79 (± 2.02) | -1.71 (± 2.16) | -0.75 (± 1.85) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in sagittal diameter after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0075 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in sagittal diameter after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0142 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in sagittal diameter after 26 weeks

| End point title | Absolute change from baseline in sagittal diameter after 26 weeks |
|---|---|

End point description:

Sagittal diameter was measured in cm (one decimal) at pre-specified visits. For measurement of the sagittal diameter, the patient lied down on his/her back while having knees bent, so that the lower back was in contact with the surface he/she was lying on. The distance from the back to the highest point of the abdomen was measured in cm while the patient exhaled.

This end-point reports the mean absolute change from baseline (Visit 2, Day 1) in sagittal diameter at Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Sagittal abdominal diameter was assessed at Visit 2 (Day 1), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: centimetre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (Week 26), pre-dose | -1.35 (± 2.22) | -1.89 (± 2.06) | -0.49 (± 2.13) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in sagittal diameter after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0522 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in sagittal diameter after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |

## Secondary: Relative (%) change from baseline in percentage body fat after 14 weeks

| End point title | Relative (%) change from baseline in percentage body fat after 14 weeks |
|---|---|

End point description:

Body composition (percentage body fat) was measured using a bio-impedance measuring device (Tanita BC-545N), according to the manufacturer's instructions, at pre-specified visits during the study.

This end-point reports the mean relative (%) change from baseline (Visit 2, Day 1) in percentage body fat after 14 weeks.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Percentage body fat was assessed at Visit 2 (Day 1) and Visit 4 (Week 14).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 47 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -0.4 (± 9.1) | -2.8 (± 6.2) | 0.5 (± 5.8) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in percentage body fat after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3682 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in percentage body fat after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0233 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in percentage body fat after 26 weeks

| | |
|---|---|
| End point title | Relative (%) change from baseline in percentage body fat after 26 weeks |

End point description:

Body composition (percentage body fat) was measured using a bio-impedance measuring device (Tanita BC-545N), according to the manufacturer's instructions, at pre-specified visits during the study.

This end-point reports the mean relative (%) change from baseline (Visit 2, Day 1) in percentage body fat after 26 weeks.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Percentage body fat was assessed at Visit 2 (Day 1) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (Week 26), pre-dose | -2.8 (± 10.2) | -5.4 (± 7.4) | -0.3 (± 7.8) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in percentage body fat after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1733 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in percentage body fat after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0047 |
| Method | ANOVA |

## Secondary: Absolute change from baseline in percentage body fat after 14 weeks

| End point title | Absolute change from baseline in percentage body fat after 14 weeks |
|---|---|

End point description:

Body composition (percentage body fat) was measured using a bio-impedance measuring device (Tanita BC-545N), according to the manufacturer's instructions, at pre-specified visits during the study.

This end-point reports the mean absolute change from baseline (Visit 2, Day 1) in percentage body fat after 14 weeks.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Percentage body fat was assessed at Visit 2 (Day 1) and Visit 4 (Week 14).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 47 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14), pre-dose | -0.40 (± 3.33) | -1.11 (± 2.24) | 0.15 (± 2.40) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in percentage of body fat after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment and body weight at

baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2727 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in percentage of body fat after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment and body weight at baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0195 |
| Method | ANCOVA |

### Secondary: Absolute change from baseline in percentage body fat after 26 weeks

| End point title | Absolute change from baseline in percentage body fat after 26 weeks |
|---|---|

End point description:

Body composition (percentage body fat) was measured using a bio-impedance measuring device (Tanita BC-545N), according to the manufacturer's instructions, at pre-specified visits during the study.

This end-point reports the mean absolute change from baseline (Visit 2, Day 1) in percentage body fat after 26 weeks.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Percentage body fat was assessed at Visit 2 (Day 1) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (Week 26), pre-dose | -1.45 (± 3.73) | -2.21 (± 2.68) | -0.19 (± 3.13) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in percentage of body fat after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment and body weight at baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0676 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in percentage of body fat after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment and body weight at baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0035 |
| Method | ANCOVA |

## Secondary: Relative change from baseline in satiety and craving after 14 weeks

| End point title | Relative change from baseline in satiety and craving after 14 weeks |
|---|---|

End point description:

The satiety and craving questionnaire consists of 7 questions about sense of hunger, sense of satiety and craving for certain types of food that need to be answered on a scale from 0 (not at all) to 9 (extremely much). At each applicable visit, the patients answered the questionnaire once prior to breakfast and 4 times after breakfast (once every hour). The total score of all questionnaires were combined in descriptive summaries. A low score indicates low appetite while a high score indicates high appetite. This end-point reports the mean relative (%) change from baseline (Visit 2, Day 1) in total score at week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

The satiety and craving questionnaires were filled in by the patients at Visit 2 (Day1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26). The questionnaires were fillid in before breakfast, then every hour for 4 hours until lunch.

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 38 | 37 | 35 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 4 (week 14) | 3.2 (± 34.6) | 1.5 (± 27.9) | -1.1 (± 34.1) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|
| Statistical analysis description: | |

The Satiety and craving questionnaire includes 7 questions, with a scale 0 (not at all) to 9 (extremely much). The second and third question in the questionnaire were reversed before calculating the total score. Satiety and craving as total score after 14 weeks of treatment with EMP16-120/40 as compared to placebo, corrected for hunger and craving after standardised breakfast at baseline, was analyzed using the Wilcoxon Rank Sum test.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6389 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|
| Statistical analysis description: | |

The Satiety and craving questionnaire includes 7 questions, with a scale 0 (not at all) to 9 (extremely much). The second and third question in the questionnaire were reversed before calculating the total score. Satiety and craving as total score after 14 weeks of treatment with EMP16-150/50 as compared to placebo, corrected for hunger and craving after standardised breakfast at baseline, was analyzed using the Wilcoxon Rank Sum test.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 72 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7017 |
| Method | Wilcoxon (Mann-Whitney) |

## Secondary: Relative change from baseline in satiety and craving after 26 weeks

| End point title | Relative change from baseline in satiety and craving after 26 weeks |
|---|---|

End point description:

The satiety and craving questionnaire consists of 7 questions about sense of hunger, sense of satiety and craving for certain types of food that need to be answered on a scale from 0 (not at all) to 9 (extremely much). At each applicable visit, the patients answered the questionnaire once prior to breakfast and 4 times after breakfast (once every hour). The total score of all questionnaires were combined in descriptive summaries. A low score indicates low appetite while a high score indicates high appetite. This end-point reports the mean relative (%) change from baseline (Visit 2, Day 1) in total score at week 14.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

The satiety and craving questionnaires were filled in by the patients at Visit 2 (Day1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26). The questionnaires were fillid in before breakfast, then every hour for 4 hours until lunch.

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 35 | 34 | 38 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 5 (Week 26) | 12.7 (± 40.3) | 3.6 (± 34.0) | 3.3 (± 37.7) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The Satiety and craving questionnaire includes 7 questions, with a scale 0 (not at all) to 9 (extremely much). The second and third question in the questionnaire were reversed before calculating the total score. Satiety and craving as total score after 26 weeks of treatment with EMP16-120/40 as compared to placebo, corrected for hunger and craving after standardised breakfast at baseline, was analyzed using the Wilcoxon Rank Sum test.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1762 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The Satiety and craving questionnaire includes 7 questions, with a scale 0 (not at all) to 9 (extremely much). The second and third question in the questionnaire were reversed before calculating the total score. Satiety and craving as total score after 26 weeks of treatment with EMP16-150/50 as compared to placebo, corrected for hunger and craving after standardised breakfast at baseline, was analyzed

using the Wilcoxon Rank Sum test.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 72 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9057 |
| Method | Wilcoxon (Mann-Whitney) |

## Secondary: Relative (%) change from baseline in fasting albumin after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting albumin after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting albumin after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[17] | 50[18] | 50[19] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 1.4 (± 7.4) | 1.9 (± 7.2) | -0.5 (± 6.3) | |
| VISIT 4 (WEEK 14), PREDOSE | -1.3 (± 4.5) | -2.2 (± 7.2) | -3.5 (± 5.3) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.3 (± 5.8) | -0.4 (± 7.2) | -0.8 (± 6.0) | |

Notes:

[17] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[18] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[19] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1787 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 7 weeks of treatment with or EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | Placebo v EMP16-02 - 150/50 |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0897 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 94 (the number 98 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0447 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 96 (the number 100 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1122 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3186 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting albumin after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3509 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting glucose after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting glucose after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting glucose after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|
| End point timeframe: | |

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[20] | 50[21] | 50[22] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -2.3 (± 7.2) | -2.5 (± 9.9) | -1.4 (± 6.2) | |
| VISIT 4 (WEEK 14), PREDOSE | -4.5 (± 7.9) | -4.2 (± 8.9) | -2.4 (± 6.6) | |
| VISIT 5 (WEEK 26), PREDOSE | -4.2 (± 8.2) | -4.1 (± 10.4) | -2.4 (± 7.6) | |

Notes:

[20] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[21] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[22] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting glucose after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5665 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting glucose after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4785 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting glucose after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.208 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting glucose after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2512 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting glucose after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4333 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting glucose after 26 weeks of treatment with EMP16-

150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4537 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[23] | 50[24] | 50[25] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -3.9 (± 5.7) | -2.5 (± 4.6) | -1.7 (± 3.9) | |
| VISIT 4 (WEEK 14), PREDOSE | -2.1 (± 5.5) | -0.6 (± 5.3) | 0.2 (± 5.3) | |
| VISIT 5 (WEEK 26), PREDOSE | -3.1 (± 5.8) | -2.8 (± 6.1) | -1.5 (± 5.8) | |

Notes:

[23] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[24] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[25] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.022 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3992 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0252 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3543 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0753 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HbA1c after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1711 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting insulin after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting insulin after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting insulin after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|
| End point timeframe: | |

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[26] | 49[27] | 50[28] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -15.0 (± 29.7) | -13.6 (± 37.4) | -8.0 (± 33.2) | |
| VISIT 4 (WEEK 14), PREDOSE | -15.9 (± 32.1) | -13.7 (± 39.1) | 5.1 (± 49.6) | |
| VISIT 5 (WEEK 26), PREDOSE | -9.1 (± 35.8) | 7.5 (± 106.9) | 0.6 (± 48.8) | |

Notes:

[26] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[27] - n=49 for week 7, n=46 for week 14 and n=43 for week 26

[28] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting insulin after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3037 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting insulin after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4097 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting insulin after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0096 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting insulin after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 95 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0192 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting insulin after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4187 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting insulin after 26 weeks of treatment with EMP16-150/50

as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7561 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting triglycerides after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting triglycerides after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting triglycerides after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[29] | 50[30] | 49[31] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 7.3 (± 32.8) | 6.3 (± 41.0) | -3.6 (± 29.0) | |
| VISIT 4 (WEEK 14), PREDOSE | -2.5 (± 28.3) | 1.2 (± 38.4) | -8.3 (± 36.2) | |
| VISIT 5 (WEEK 26), PREDOSE | 2.4 (± 37.6) | 5.0 (± 46.0) | -8.6 (± 28.3) | |

Notes:

[29] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[30] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[31] - n=49 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1252 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1613 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 94 (the number 97 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6082 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 96 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 99 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1851 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 90 (the number 97 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.368 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting triglycerides after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 91 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.122 |
| Method | ANOVA |

### Secondary: Relative (%) change from baseline in fasting LDL cholesterol after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting LDL cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting low-density lipoprotein (LDL) cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|
| End point timeframe: | |

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[32] | 50[33] | 50[34] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -12.2 (± 13.0) | -9.5 (± 13.3) | 0.1 (± 16.8) | |
| VISIT 4 (WEEK 14), PREDOSE | -13.8 (± 12.8) | -9.0 (± 19.5) | -3.1 (± 17.7) | |
| VISIT 5 (WEEK 26), PREDOSE | -8.8 (± 13.7) | -7.4 (± 15.3) | 1.8 (± 18.5) | |

Notes:

[32] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[33] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[34] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting LDL cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The relative (%) change from baseline in fasting LDL cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0012 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting LDL cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0038 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting LDL cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.082 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting LDL cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0017 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting LDL cholesterol after 26 weeks of treatment with

EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0028 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting HDL cholesterol after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting HDL cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting high-density lipoprotein (HDL) cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[35] | 50[36] | 50[37] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -10.4 (± 10.4) | -11.2 (± 10.8) | 2.5 (± 14.4) | |
| VISIT 4 (WEEK 14), PREDOSE | -9.8 (± 11.3) | -13.5 (± 11.4) | -0.8 (± 13.1) | |
| VISIT 5 (WEEK 26), PREDOSE | -7.6 (± 12.0) | -10.9 (± 12.3) | -0.3 (± 12.8) | |

Notes:

[35] - n=48 for week 7, n=45 for week 14 and n=44 for week 26

[36] - n=50 for week 7, n=47 for week 14 and n=45 for week 26

[37] - n=50 for week 7, n=49 for week 14 and n=46 for week 26

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0005 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0038 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting HDL cholesterol after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in this analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting total cholesterol after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting total cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting total cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[38] | 50[39] | 50[40] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
|     VISIT 3 (WEEK 7), PREDOSE | -9.4 (± 10.9) | -8.8 (± 10.2) | 0.4 (± 10.1) | |
|     VISIT 4 (WEEK 14), PREDOSE | -12.2 (± 10.5) | -9.7 (± 12.7) | -3.6 (± 11.1) | |
|     VISIT 5 (WEEK 26), PREDOSE | -8.6 (± 11.4) | -8.0 (± 12.5) | -2.2 (± 11.3) | |

Notes:

[38] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[39] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[40] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0047 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting total cholesterol after 26 weeks of treatment with

EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0021 |
| Method | ANOVA |

### Secondary: Relative (%) change from baseline in fasting hs-CRP after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting hs-CRP after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting high-sensitivity C-reactive protein (hs-CRP) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[41] | 50[42] | 50[43] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 26.5 (± 200.5) | 10.2 (± 91.7) | 42.2 (± 321.7) | |
| VISIT 4 (WEEK 14), PREDOSE | -5.6 (± 60.5) | 12.6 (± 134.3) | 38.2 (± 241.1) | |
| VISIT 5 (WEEK 26), PREDOSE | 7.2 (± 106.0) | -19.5 (± 37.0) | 5.8 (± 65.8) | |

Notes:

[41] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[42] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[43] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

### Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7314 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4793 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2511 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.425 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6908 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting hs-CRP after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0665 |
| Method | ANOVA |

## Secondary: Absolute change from baseline in fasting albumin after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting albumin after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting albumin after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[44] | 50[45] | 50[46] | |
| Units: g/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 0.5 (± 3.0) | 0.6 (± 2.8) | -0.2 (± 2.5) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.6 (± 1.9) | -1.0 (± 2.9) | -1.4 (± 2.1) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.2 (± 2.4) | -0.2 (± 2.9) | -0.3 (± 2.4) | |

Notes:

[44] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[45] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[46] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1607 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1098 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0775 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3853 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9178 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting albumin after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9943 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in fasting glucose after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting glucose after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting glucose after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[47] | 50[48] | 50[49] | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.16 (± 0.45) | -0.17 (± 0.63) | -0.10 (± 0.40) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.30 (± 0.50) | -0.27 (± 0.55) | -0.15 (± 0.45) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.27 (± 0.50) | -0.26 (± 0.65) | -0.16 (± 0.49) | |

Notes:

[47] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[48] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[49] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| Number of subjects included in analysis | 98 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.478 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.426 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1858 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2475 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3422 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting glucose after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3651 |
| Method | ANCOVA |

### Secondary: Absolute change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting hemoglobin A1C (HbA1c) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[50] | 50[51] | 50[52] | |
| Units: mmol/mol | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -1.5 (± 2.3) | -0.9 (± 1.7) | -0.7 (± 1.4) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.9 (± 2.3) | -0.3 (± 1.9) | 0.0 (± 1.9) | |
| VISIT 5 (WEEK 26), PREDOSE | -1.2 (± 2.3) | -1.1 (± 2.4) | -0.6 (± 2.2) | |

Notes:

[50] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[51] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[52] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.


## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting HbA1c after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0283 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting HbA1c after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5118 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting HbA1c after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |

The total number of subjects ncluded in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0667 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HbA1c after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects ncluded in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5837 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HbA1c after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects ncluded in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2908 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HbA1c after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects ncluded in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3418 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in fasting insulin after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting insulin after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting insulin after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[53] | 49[54] | 50[55] | |
| Units: mIU/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -3.958 (± 8.125) | -3.129 (± 8.642) | -3.320 (± 10.68) | |
| VISIT 4 (WEEK 14), PREDOSE | -4.222 (± 7.674) | -3.241 (± 7.919) | -0.01020 (± 11.83) | |
| VISIT 5 (WEEK 26), PREDOSE | -3.620 (± 9.705) | 0.07907 (± 18.10) | -1.509 (± 8.411) | |

Notes:

[53] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[54] - n=49 for week 7, n=46 for week 14 and n=43 for week 26.

[55] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting insulin after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6382 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting insulin after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9784 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting insulin after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in this analysis was 94 (the number 98 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0358 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting insulin after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in this analysis was 95 (the number 99 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1012 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |

Statistical analysis description:

The absolute change from baseline in fasting insulin after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in this analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3965 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |

Statistical analysis description:

The absolute change from baseline in fasting insulin after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in this analysis was 89 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5905 |
| Method | ANCOVA |

### Secondary: Absolute change from baseline in fasting triglycerides after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting triglycerides after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting triglycerides after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[56] | 50[57] | 49[58] | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 0.011 (± 0.632) | -0.047 (± 0.619) | -0.149 (± 0.659) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.116 (± 0.483) | -0.070 (± 0.623) | -0.275 (± 0.732) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.092 (± 0.642) | -0.028 (± 0.626) | -0.237 (± 0.784) | |

Notes:

[56] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[57] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[58] - n=49 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2494 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4506 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 97 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3274 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1452 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 97 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4394 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting triglycerides after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 99 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1912 |
| Method | ANCOVA |

**Secondary: Absolute change from baseline in fasting LDL cholesterol after 7, 14 and 26 weeks**

| End point title | Absolute change from baseline in fasting LDL cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting low-density lipoprotein (LDL) cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[59] | 50[60] | 50[61] | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.49 (± 0.52) | -0.34 (± 0.52) | -0.05 (± 0.51) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.51 (± 0.46) | -0.36 (± 0.66) | -0.14 (± 0.51) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.34 (± 0.52) | -0.26 (± 0.61) | 0.01 (± 0.55) | |

Notes:

[59] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[60] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[61] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| Number of subjects included in analysis | 98 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0051 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0473 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0024 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting LDL cholesterol after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0203 |
| Method | ANCOVA |

### Secondary: Absolute change from baseline in fasting HDL cholesterol after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting HDL cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting high-density lipoprotein (HDL) cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[62] | 50[63] | 50[64] | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.15 (± 0.14) | -0.16 (± 0.16) | 0.03 (± 0.19) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.14 (± 0.15) | -0.20 (± 0.19) | -0.02 (± 0.19) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.11 (± 0.16) | -0.16 (± 0.19) | -0.02 (± 0.18) | |

Notes:

[62] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[63] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[64] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.


## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0015 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0253 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting HDL cholesterol after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | ANCOVA |

**Secondary: Absolute change from baseline in fasting cholesterol after 7, 14 and 26 weeks**

| End point title | Absolute change from baseline in fasting cholesterol after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting total cholesterol after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[65] | 50[66] | 50[67] | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.59 (± 0.82) | -0.48 (± 0.59) | 0.00 (± 0.53) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.72 (± 0.70) | -0.56 (± 0.76) | -0.22 (± 0.56) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.53 (± 0.73) | -0.45 (± 0.76) | -0.13 (± 0.59) | |

Notes:

[65] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[66] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[67] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| Number of subjects included in analysis | 98 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0005 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0004 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0142 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0069 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting total cholesterol after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0297 |
| Method | ANCOVA |

### Secondary: Absolute change from baseline in fasting hs-CRP after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting hs-CRP after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting high-sensitivity C-reactive protein (hs-CRP) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[68] | 50[69] | 50[70] | |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.7 (± 3.2) | 0.1 (± 2.6) | -0.2 (± 7.5) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.7 (± 3.1) | -0.7 (± 2.8) | -0.3 (± 7.3) | |
| VISIT 5 (WEEK 26), PREDOSE | 0.7 (± 11.0) | -1.1 (± 2.0) | -0.6 (± 6.6) | |

Notes:

[68] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[69] - n=50 for week 7, n=47 for week 14 and n=45 for week 26.

[70] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting hs-CRP after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7331 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting hs-CRP after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6953 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting hs-CRP after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8853 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting hs-CRP after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 96 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7778 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting hs-CRP after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3464 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting hs-CRP after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8254 |
| Method | ANCOVA |

## Secondary: Relative (%) change from baseline in fasting ALT after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting ALT after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting alanine aminotransferase (ALT) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[71] | 50[72] | 50[73] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 10.8 (± 51.5) | 8.0 (± 38.5) | -6.7 (± 27.6) | |
| VISIT 4 (WEEK 14), PREDOSE | 3.0 (± 35.3) | 17.6 (± 85.5) | -3.2 (± 55.6) | |
| VISIT 5 (WEEK 26), PREDOSE | -4.5 (± 36.9) | 3.6 (± 49.6) | -7.7 (± 27.9) | |

Notes:

[71] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[72] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[73] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| Number of subjects included in analysis | 98 |
| --- | --- |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0333 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
| --- | --- |

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
| --- | --- |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0707 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
| --- | --- |

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
| --- | --- |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6289 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
| --- | --- |

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
| --- | --- |

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1126 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9673 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALT after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6607 |
| Method | ANOVA |

| **Secondary: Relative (%) change from baseline in fasting AST after 7, 14 and 26 weeks** | |
|---|---|
| End point title | Relative (%) change from baseline in fasting AST after 7, 14 and 26 weeks |

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting aspartate aminotransferase (AST) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
| --- | --- |

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
| --- | --- | --- | --- | --- |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47[74] | 50[75] | 48[76] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 4.2 (± 28.7) | 4.9 (± 26.1) | -2.7 (± 31.8) | |
| VISIT 4 (WEEK 14), PREDOSE | -4.5 (± 21.2) | 22.5 (± 183.8) | -11.2 (± 22.2) | |
| VISIT 5 (WEEK 26), PREDOSE | -7.3 (± 22.2) | 0.9 (± 34.4) | -4.5 (± 27.6) | |

Notes:

[74] - n=47 for week 7, n=44 for week 14 and n=43 for week 26.

[75] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[76] - n=48 for week 7, n=49 for week 14 and n=46 for week 26.

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
| --- | --- |

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
| --- | --- |
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2479 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
| --- | --- |

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
| --- | --- |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1949 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the anlaysis was 93 (the number 95 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7191 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the anlaysis was 95 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1281 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the anlaysis was 89 (the number 95 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8387 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting AST after 26 weeks of treatment with EMP16-150/50 as

compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the anlaysis was 91 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3571 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting ALP after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting ALP after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting alkaline phosphatase (ALP) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[77] | 50[78] | 50[79] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 3.3 (± 10.4) | 0.6 (± 10.7) | -0.8 (± 10.9) | |
| VISIT 4 (WEEK 14), PREDOSE | 3.8 (± 10.7) | 1.0 (± 13.8) | -0.9 (± 12.3) | |
| VISIT 5 (WEEK 26), PREDOSE | 8.5 (± 14.9) | 3.7 (± 15.1) | 2.4 (± 11.4) | |

Notes:

[77] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[78] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[79] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0608 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5028 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0717 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3449 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0618 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting ALP after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.916 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in fasting GGT after 7, 14 and 26 weeks

| End point title | Relative (%) change from baseline in fasting GGT after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean relative (%) change from baseline in fasting gamma glutamyl transferase (GGT) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[80] | 50[81] | 50[82] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -5.3 (± 21.1) | -6.1 (± 20.2) | -1.5 (± 28.3) | |
| VISIT 4 (WEEK 14), PREDOSE | -10.5 (± 41.6) | -2.0 (± 46.1) | -1.6 (± 44.0) | |
| VISIT 5 (WEEK 26), PREDOSE | -9.6 (± 38.2) | -12.2 (± 23.5) | -2.0 (± 31.7) | |

Notes:

[80] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[81] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[82] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4247 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3328 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3522 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8695 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1313 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in fasting GGT after 26 weeks of treatment with EMP16-150/50

as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0334 |
| Method | ANOVA |

## Secondary: Absolute change from baseline in fasting ALT after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting ALT after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting alanine aminotransferase (ALT) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[83] | 50[84] | 50[85] | |
| Units: ukat/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 0.024 (± 0.242) | 0.020 (± 0.234) | -0.056 (± 0.188) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.026 (± 0.204) | 0.043 (± 0.366) | -0.063 (± 0.202) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.057 (± 0.217) | -0.015 (± 0.313) | -0.069 (± 0.151) | |

Notes:

[83] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[84] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[85] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body

weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0735 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0878 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4925 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0555 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8744 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALT after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3057 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in fasting AST after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting AST after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting aspartate aminotransferase (AST) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47[86] | 50[87] | 48[88] | |
| Units: ukat/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 0.010 (± 0.127) | 0.011 (± 0.128) | -0.040 (± 0.150) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.034 (± 0.105) | 0.076 (± 0.721) | -0.072 (± 0.143) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.046 (± 0.112) | -0.012 (± 0.138) | -0.037 (± 0.137) | |

Notes:

[86] - n=47 for week 7, n=44 for week 14 and n=43 for week 26.

[87] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[88] - n=48 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting AST after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0915 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |
| The absolute change from baseline in fasting AST after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0674 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting AST after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 93 (the number 95 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6081 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting AST after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 95 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0863 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting AST after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 89 (the number 95 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6796 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting AST after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3852 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in fasting ALP after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting ALP after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting alkaline phosphatase (ALP) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[89] | 50[90] | 50[91] | |
| Units: ukat/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | 0.031 (± 0.136) | -0.003 (± 0.128) | -0.016 (± 0.121) | |
| VISIT 4 (WEEK 14), PREDOSE | 0.035 (± 0.135) | -0.001 (± 0.163) | -0.021 (± 0.141) | |
| VISIT 5 (WEEK 26), PREDOSE | 0.090 (± 0.178) | 0.036 (± 0.178) | 0.013 (± 0.134) | |

Notes:

[89] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[90] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[91] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALP after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | Placebo v EMP16-02 - 120/40 |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0675 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALP after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5983 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALP after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0823 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting ALP after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5335 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |

Statistical analysis description:

The absolute change from baseline in fasting ALP after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0367 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |

Statistical analysis description:

The absolute change from baseline in fasting ALP after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5585 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in fasting GGT after 7, 14 and 26 weeks

| End point title | Absolute change from baseline in fasting GGT after 7, 14 and 26 weeks |
|---|---|

End point description:

Venous blood samples (4 mL) were collected to analyze the fasting profile of lipid metabolism markers, glucose metabolism markers, and inflammation markers. All parameters were analyzed in immediate association with sampling. This end-point reports the mean absolute change from baseline in fasting gamma glutamyl transferase (GGT) after 7, 14 and 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis was done at Visit 2 (Day 1, baseline), Visit 3 (Week 7), Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 48[92] | 50[93] | 50[94] | |
| Units: ukat/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 3 (WEEK 7), PREDOSE | -0.02958 (± 0.1519) | -0.04700 (± 0.1923) | -0.09420 (± 0.4697) | |
| VISIT 4 (WEEK 14), PREDOSE | -0.06933 (± 0.1948) | -0.01826 (± 0.2228) | -0.09367 (± 0.4742) | |
| VISIT 5 (WEEK 26), PREDOSE | -0.07318 (± 0.2006) | -0.07111 (± 0.1611) | -0.1226 (± 0.5147) | |

Notes:

[92] - n=48 for week 7, n=45 for week 14 and n=44 for week 26.

[93] - n=50 for week 7, n=46 for week 14 and n=45 for week 26.

[94] - n=50 for week 7, n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in fasting GGT after 7 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.22 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in fasting GGT after 7 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3775 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|
| Statistical analysis description: | |

The absolute change from baseline in fasting GGT after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 94 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6703 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting GGT after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 95 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2478 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting GGT after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 98 refers to week 7).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4007 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in fasting GGT after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 91 (the number 100 refers to week 7).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| Number of subjects included in analysis | 100 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.41 |
| Method | ANCOVA |

## Secondary: Diabetic status at baseline, week 14 and week 26

| End point title | Diabetic status at baseline, week 14 and week 26 |
|---|---|

End point description:

Diabetic status was defined as fasting glucose ≥ 7.0 mmol/L and prediabetic status was defined as fasting glucose ≥ 6.1 mmol/L and < 7.0 mmol/L. This end-point reports the proportions (%) of diabetic, non-diabetic and prediabetic patients at baseline (Week 1, Day 1), Week 14 and Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood sampling for analysis of fasting glucose was done at Visit 2 (Day 1, baseline), Visit 4 (Week 14) and Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52[95] | 52[96] | 52[97] | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| VISIT 2 (WEEK 1), PREDOSE - Diabetic | 9.6 | 3.8 | 9.6 | |
| VISIT 2 (WEEK 1), PREDOSE - Non-diabetic | 65 | 69 | 54 | |
| VISIT 2 (WEEK 1), PREDOSE - Prediabetic | 25 | 27 | 37 | |
| VISIT 4 (WEEK 14), PREDOSE - Diabetic | 2.2 | 4.3 | 16 | |
| VISIT 4 (WEEK 14), PREDOSE - Non-diabetic | 80 | 81 | 67 | |
| VISIT 4 (WEEK 14), PREDOSE - Prediabetic | 18 | 15 | 16 | |
| VISIT 5 (WEEK 26), PREDOSE - Diabetic | 4.5 | 2.2 | 13 | |
| VISIT 5 (WEEK 26), PREDOSE - Non-diabetic | 75 | 76 | 65 | |
| VISIT 5 (WEEK 26), PREDOSE - Prediabetic | 20 | 22 | 22 | |

Notes:

[95] - n=52 for Week 1 (baseline), n=45 for week 14 and n=44 for week 26.

[96] - n=52 for Week 1 (baseline), n=47 for week 14 and n=45 for week 26.

[97] - n=52 for Week 1 (baseline), n=49 for week 14 and n=46 for week 26.

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The change from baseline in the proportion of diabetic and prediabetic patients after 14 weeks of treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction.

The total number of subjects included in the analysis was 94 (the number 104 refers to Week 1).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0667 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The change from baseline in the proportion of diabetic and prediabetic patients after 14 weeks of treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction.

The total number of subjects included in the analysis was 96 (the number 104 refers to Week 1).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1368 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The change from baseline in the proportion of diabetic and prediabetic patients after 26 weeks of treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction.

The total number of subjects included in the analysis was 90 (the number 104 refers to Week 1).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3409 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The change from baseline in the proportion of diabetic and prediabetic patients after 26 weeks of treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction.

The total number of subjects included in the analysis was 91 (the number 104 refers to Week 1).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1488 |
| Method | Chi-squared |

## Secondary: Relative (%) change from baseline in systolic blood pressure after 14 weeks

| End point title | Relative (%) change from baseline in systolic blood pressure after 14 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean relative (%) change from baseline in systolic blood pressure after 14 weeks of treatment. The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 4 (Week 14).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 4 (WEEK 14), PRE-DOSE | -1.9 (± 7.5) | -4.7 (± 9.5) | -1.4 (± 6.9) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in systolic and diastolic blood pressure, after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4224 |
| Method | ANOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in systolic and diastolic blood pressure, after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0273 |
| Method | ANOVA |

### Secondary: Relative (%) change from baseline in systolic blood pressure after 26 weeks

| End point title | Relative (%) change from baseline in systolic blood pressure after 26 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean relative (%) change from baseline in systolic blood pressure after 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 5 (WEEK 26), PRE-DOSE | -1.7 (± 8.8) | -3.2 (± 9.2) | -1.1 (± 8.4) | |

### Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in systolic blood pressure after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2631 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in systolic blood pressure after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0505 |
| Method | ANOVA |

## Secondary: Absolute change from baseline in systolic blood pressure after 14 weeks

| End point title | Absolute change from baseline in systolic blood pressure after 14 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean absolute change from baseline in systolic blood pressure after 14 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 4 (Week 14).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 4 (WEEK 14), PRE-DOSE | -2.6 (± 9.9) | -6.9 (± 13.4) | -2.2 (± 8.9) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7327 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.03 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in systolic blood pressure after 26 weeks

| End point title | Absolute change from baseline in systolic blood pressure after 26 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean absolute change from baseline in systolic blood pressure after 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 5 (WEEK 26), PRE-DOSE | -2.7 (± 12.0) | -4.9 (± 13.6) | -1.8 (± 11.2) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in systolic blood pressure after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5771 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in systolic blood pressure after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1822 |
| Method | ANCOVA |

## Secondary: Relative (%) change from baseline in diastolic blood pressure after 14 weeks

| End point title | Relative (%) change from baseline in diastolic blood pressure after 14 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean relative (%) change from baseline in diastolic blood pressure after 14 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 4 (Week 14).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 4 (WEEK 14), PRE-DOSE | -3.2 (± 8.2) | -3.3 (± 10.1) | 0.6 (± 7.1) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0215 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0284 |
| Method | ANOVA |

## Secondary: Relative (%) change from baseline in diastolic blood pressure after 26 weeks

| End point title | Relative (%) change from baseline in diastolic blood pressure after 26 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean relative (%) change from baseline in diastolic blood pressure after 26 weeks of treatment. 2

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 5 (Week 26).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 5 (WEEK 26), PRE-DOSE | -3.3 (± 8.1) | -2.8 (± 9.3) | -1.4 (± 8.7) | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in diastolic blood pressure after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1509 |
| Method | ANOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The relative (%) change from baseline in diastolic blood pressure after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANOVA with treatment as independent variable. Data underlying the ANOVA has been imputated in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | Placebo v EMP16-02 - 150/50 |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.148 |
| Method | ANOVA |

**Secondary: Absolute change from baseline in diastolic blood pressure after 14 weeks**

| | |
|---|---|
| End point title | Absolute change from baseline in diastolic blood pressure after 14 weeks |

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean absolute change from baseline in diastolic blood pressure after 14 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 4 (Week 14).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 49 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 4 (WEEK 14), PRE-DOSE | -2.8 (± 7.0) | -3.3 (± 8.7) | 0.2 (± 5.9) | |

**Statistical analyses**

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0542 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 14 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0221 |
| Method | ANCOVA |

## Secondary: Absolute change from baseline in diastolic blood pressure after 26 weeks

| End point title | Absolute change from baseline in diastolic blood pressure after 26 weeks |
|---|---|

End point description:

Systolic and diastolic blood pressure were measured in supine position after 10 minutes of rest. This end-point reports the mean absolute change from baseline in diastolic blood pressure after 26 weeks of treatment.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Blood pressure was assessed at Visit 2 (Day 1, baseline) and at Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44 | 45 | 46 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| VISIT 5 (WEEK 26), PRE-DOSE | -3.0 (± 7.0) | -3.0 (± 8.1) | -1.5 (± 7.3) | |

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 26 weeks of treatment with EMP16-120/40 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3769 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in diastolic blood pressure after 26 weeks of treatment with EMP16-150/50 as compared to placebo was analyzed using ANCOVA with treatment as independent variable and body weight at baseline as covariates. Data underlying the ANCOVA has been imputed in case of missing values using Last Observation Carried Forward, LOCF.

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.384 |
| Method | ANCOVA |

## Secondary: Relative (%) change from baseline in quality of life after 26 weeks

| End point title | Relative (%) change from baseline in quality of life after 26 weeks |
|---|---|

End point description:

The RAND-36 health questionnaire comprises 36 questions. The questionnaire taps eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perception. It also includes a single item that provides an indication of perceived change in health. A low score indicates poor healthrelated quality of life while a high score indicates good health-related quality of life.

This end-point reports the mean relative (%) change from baseline (Week 1, Day 1) in score mean for the 8 health concepts scales and for the additional "Health Transition Score" included in the questionnaire, at week 26. The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

The RAND-36 health questionnaire was filled in by the subjects at Visit 2 (Day 1, baseline) and at Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 42[98] | 41[99] | 47[100] | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| 1. Physical functioning Mean - Week 26 | 30.1 (± 110.8) | 22.5 (± 38.2) | 3.8 (± 17.7) | |
| 2. Role functioning/Physical Mean - Week 26 | 19.4 (± 75.7) | 35.4 (± 93.4) | 6.9 (± 59.5) | |

| | | | |
|---|---|---|---|
| 3. Pain (Bodily Pain) Mean -Week 26 | 5.6 (± 30.1) | 23.4 (± 44.1) | 2.8 (± 34.1) |
| 4. General health Mean -Week 26 | 12.6 (± 48.5) | 10.8 (± 21.4) | -5.2 (± 19.8) |
| 5. Energy/fatigue (Vitality) Mean - Week 26 | 21.8 (± 114.2) | 33.0 (± 102.3) | -3.0 (± 28.0) |
| 6. Social Functioning Mean - Week 26 | 5.0 (± 31.6) | 28.2 (± 90.3) | 0.7 (± 25.9) |
| 7. Role functioning/Emotional Mean - Week 26 | -4.7 (± 47.0) | 10.1 (± 76.6) | -13.7 (± 35.8) |
| 8. Emotional wellbeing (Mental) Mean - Week 26 | -0.8 (± 29.0) | 5.9 (± 34.4) | -4.9 (± 15.1) |
| 9. Health Transition score Mean - Week 26 | 41.3 (± 63.3) | 48.4 (± 65.2) | 13.0 (± 36.5) |

Notes:

[98] - n=42 for scale no 1, 3-6 & 8
n=39 for scale no 2 & 7
n=40 for scale no 9
[99] - n=41 for scale no 1
n=40 for scale no 2 & 9
n=41 for scale no 3-6 & 8
n=38 for scale no 7
[100] - n=47 for scale no 1, 3, 4, 6 & 8
n=46 for scale no 2, 5 & 9
n=45 for scale no 7

## Statistical analyses

| Statistical analysis title | Scale no 1 - EMP16-120/40 VS placebo |
|---|---|
| Statistical analysis description: | |

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 1 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0131 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 1 - EMP16-150/50 VS placebo |
|---|---|
| Statistical analysis description: | |

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 1 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0024 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 2 - EMP16-120/40 VS placebo |
|---|---|
| Statistical analysis description: | |

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value

(Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 2 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 85 (the number 89 refers to scale no 1).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2972 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 2 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 2 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 86 (the number 88 refers to scale no 1).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0923 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 3 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 3 of the RAND-36 questionnaire.

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8938 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 3 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 3 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 88 (the number 89 refers to scale no 1).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |

| Number of subjects included in analysis | 88 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0278 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 4 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 4 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.018 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 4 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 4 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0006 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 5 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 5 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 88 (the number 89 refers to scale no 1).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4296 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 5 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 5 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 87 (the number 88 refers to scale no 1).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0287 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 6 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 6 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5647 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 6 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 6 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0933 |
| Method | Wilcoxon (Mann-Whitney) |

| Statistical analysis title | Scale no 7 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 7 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 84 (the number 89 refers to scale no 1).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|

| Number of subjects included in analysis | 89 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3628 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 7 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 7 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 83 (the number 88 refers to scale no 1).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2153 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 8 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 8 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2484 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 8 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 8 of the RAND-36 questionnaire.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.039 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 9 - EMP16-120/40 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 9 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 86 (the number 89 refers to scale no 1).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0138 |
| Method | Wilcoxon (Mann-Whitney) |

| **Statistical analysis title** | Scale no 9 - EMP16-150/50 VS placebo |
|---|---|

Statistical analysis description:

The RAND-36 QoL questionnaire was analyzed in accordance with the manual. Between groups p-value (Wilcoxon) was compared between EMP16-02 and placebo. This statistical analysis regards scale no 9 of the RAND-36 questionnaire.

The total number of subjects included in the analysis was 87 (the number 88 refers to scale no 1).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0057 |
| Method | Wilcoxon (Mann-Whitney) |

### Secondary: Overall drop-out rate - Week 28

| End point title | Overall drop-out rate - Week 28 |
|---|---|

End point description:

This end-point reports the cumulative overall drop-out rate (rate of early discontinuations) at the Safety follow-up Visit (Week 28). Subjects who missed one or several visits and who later re-entered the study were not considered drop-outs until they missed all remaining visits.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Collection of reasons for early discontinuations was done from Visit 1 Screening to Visit 6 (Week 28).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52 | 52 | 52 | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| Withdrawal overall - Week 28 | 15.4 | 13.5 | 11.5 | |

**Statistical analyses**

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 28 |
|---|---|
| Statistical analysis description: | |
| The overall drop-out rate following treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5656 |
| Method | Chi-squared |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 28 |
|---|---|
| Statistical analysis description: | |
| The overall drop-out rate following treatment with EMP16-02 as compared to placebo was analyzed using Chi-square test without continuity correction. | |
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7668 |
| Method | Chi-squared |

**Secondary: GI related drop-out rate - Week 28**

| End point title | GI related drop-out rate - Week 28 |
|---|---|
| End point description: | |
| This end-point reports the cumulative gastrointestinal (GI) related drop-out rate (rate of early discontinuations) at the Safety follow-up Visit (Week 28). Subjects who missed one or several visits and who later re-entered the study were not considered drop-outs until they missed all remaining visits. | |
| The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data. | |
| End point type | Secondary |
| End point timeframe: | |
| Collection of reasons for early discontinuations was done from Visit 1 Screening to Visit 6 (Week 28). | |

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52 | 52 | 52 | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| GI related withdrawal - Week 28 | 7.7 | 9.6 | 0.0 | |

## Statistical analyses

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 28 |
|---|---|
| Statistical analysis description: | |

The GI related drop-out rate following treatment with EMP16-120/40 as compared to placebo was analyzed using Chi-square test without continuity correction.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0414 |
| Method | Chi-squared |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 28 |
|---|---|
| Statistical analysis description: | |

The GI related drop-out rate following treatment with EMP16-150/50 as compared to placebo was analyzed using Chi-square test without continuity correction.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0219 |
| Method | Chi-squared |

## Secondary: Frequency, seriousness, severity and causality of adverse events (AEs)

| End point title | Frequency, seriousness, severity and causality of adverse events (AEs) |
|---|---|
| End point description: | |

This end-point reports frequency, seriousness, severity and causality of adverse events (AEs) and serious AEs (SAEs). The grading of the severity/intensity (grade 1 to grade 5) of AEs followed the common terminology criteria for AEs (CTCAE) v5.0. AEs were assessed as unlikely, possibly or probably related to the IMP.

GI symptoms were recorded using the Gastrointestinal symptom rating scale (GSRS) questionnaire. Only symptoms assessed by the Investigator as severe (either spontaneously reported or reported in

the GSRS questionnaire) were recorded as AEs unless the GI symptom led to an early withdrawal.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

AEs (including serious AEs [SAEs]) were collected from the start of IMP administration until the end-of-study visit of each part.

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52 | 52 | 52 | |
| Units: Number of subjects | | | | |
| Any AE | 32 | 39 | 30 | |
| Any SAE | 0 | 0 | 0 | |
| Any AE leading to withdrawal | 4 | 6 | 0 | |
| Any AE leading to withdrawal of study drug | 4 | 6 | 0 | |
| Any AE leading to death | 0 | 0 | 0 | |
| Causality - Unlikely related | 22 | 28 | 27 | |
| Causality - Possibly related | 7 | 9 | 6 | |
| Causality - Probably related | 13 | 12 | 2 | |
| Severity - Mild | 21 | 24 | 22 | |
| Severity - Moderate | 11 | 13 | 11 | |
| Severity - Severe | 14 | 12 | 3 | |
| Severity - Life-threatening | 0 | 0 | 0 | |
| Severity - Death | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clinically significant (CS) abnormal findings in vital signs

| End point title | Clinically significant (CS) abnormal findings in vital signs |
|---|---|

End point description:

Systolic and diastolic blood pressure (BP) and pulse were measured in supine position after 10 minutes of rest. Vital signs were judged as normal, abnormal but not clinically significant (NCS) or abnormal and clinically significant (CS). Overall, there were no clinically relevant changes in mean systolic and diastolic BP between baseline and week 7, 14 and 26, respectively, in any treatment group. Similarly, there were no clinically relevant changes in mean pulse between the corresponding time points in any treatment group.

This end-point reports CS abnormal findings in systolic & diastolic BP and pulse.

| End point type | Secondary |
|---|---|

End point timeframe:

Vital signs were assessed at Visit 1 Screening, Visit 2 (Baseline), Visit 3 (Week 7), Visit 4 (Week 14), Visit 5 (Week 26) and Visit 6 (Week 28).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52 | 52 | 52 | |
| Units: Number of abnormal CS findings | | | | |
| CS abnormal findings in pulse | 0 | 0 | 0 | |
| CS abnormal findings in blood pressure | 0 | 0 | 0 | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Abnormal Clinically Significant findings in ECG

| End point title | Abnormal Clinically Significant findings in ECG |
|---|---|

End point description:

Single 12-lead ECGs were recorded in supine position after 10 minutes of rest using an ECG machine. Safety ECGs were reviewed and interpreted on-site by the Investigator. Any abnormalities were specified and documented in the eCRF as clinically significant (CS) or not clinically significant (NCS).

All ECGs were interpreted as normal or abnormal NCS by the Investigator at screening, week 28 or at early discontinuation end-of-study visits. There were no clinically relevant changes from baseline and no obvious differences between the treatment groups in terms of overall ECG evaluations and individual ECG parameters.

One patient in the EMP16-120/40 group reported intermittent palpitations assessed as mild and unlikely related to treatment with the IMP by the Investigator. The occurrences started almost 3 months after the first dose and lasted over a period of 26 days. The ECG of the patient was interpreted as normal both at screening and at week 28.

| End point type | Secondary |
|---|---|

End point timeframe:

ECG assessment was performed at Visit 1 Screening and at Visit 6 Safety follow-up (Week 28), or at early discontinuation end-of-study visits.

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52[101] | 52[102] | 52[103] | |
| Units: Number of abnormal CS findings | | | | |
| Abnormal CS ECG findings - Screening | 0 | 0 | 0 | |
| Abnormal CS ECG findings - Week 28 | 0 | 0 | 0 | |
| Abnormal CS ECG findings - End of Study | 0 | 0 | 0 | |

Notes:

[101] - n=52 for Screening Visit, n=44 for Week 28 and n=4 for End of study Visit

[102] - n=52 for Screening Visit, n=45 for Week 28 and n=6 for End of study Visit

[103] - n=52 for Screening Visit, n=45 for Week 28 and n=3 for End of study Visit

## Statistical analyses

No statistical analyses for this end point

---

## Secondary: Abnormal Clinically Significant findings in Clinical Chemistry

| End point title | Abnormal Clinically Significant findings in Clinical Chemistry |
|---|---|

End point description:

Blood samples for analysis of clinical chemistry parameters were collected through venipuncture and analyzed by routine analytical methods. The following parameters were analyzed: ALT, Albumin, ALP, AST, Bilirubin (total and conjugated), Calcium, Creatinine, GGT, Glucose, Hb1Ac, Phosphate, Potassium, Sodium and Urea.

Parameter values were assessed as normal, abnormal but not clinically signinficant (NCS) or abnormal and clinically significant (CS) by the Investigator.

There were no clinically relevant changes from baseline in mean clinical chemistry parameters over time and no clinically relevant differences in any laboratory parameter between any of the active treatment groups or the placebo group at any time point as assessed by the Investigator. Individual CS abnormalities were found for five patients, as reported in this end-point.

| End point type | Secondary |
|---|---|

End point timeframe:

Clinical chemistry laboratory parameters were assessed at pre-specified visits from Visit 1 Screening to Visit 6 (Week 28). In addition, for one subject an extra visit in between week 14 and week 26 was scheduled for assessment of AST.

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44[104] | 45[105] | 46[106] | |
| Units: Number of subjects | | | | |
| Abnormal CS finding - Week 26 | 1 | 1 | 1 | |
| Abnormal CS finding - Week 28 | 1 | 0 | 0 | |
| Abnormal CS finding - Extra Visit 1 subject only | 0 | 1 | 0 | |

Notes:

[104] - At Week 28, 44 subjects remained in the study. For each specific analysis n may however vary.

[105] - At Week 28, 45 subjects remained in the study. For each specific analysis n may however vary.

[106] - At Week 28, 46 subjects remained in the study. For each specific analysis n may however vary.

---

## Statistical analyses

No statistical analyses for this end point

---

## Secondary: Abnormal CS findings in hematology, coagulation and urinalysis

| End point title | Abnormal CS findings in hematology, coagulation and urinalysis |
|---|---|

End point description:

Blood samples for analysis of hematology and coagulation parameters were collected through venipuncture and analyzed by routine analytical methods. Urine analysis was performed at each research clinic using dip sticks.

Parameter values were assessed as normal, abnormal but not clinically signinficant (NCS) or abnormal and clinically significant (CS) by the Investigator.

There were no clinically relevant changes from baseline in mean hematology, coagulation or urinalysis parameters over time and no clinically relevant differences in any laboratory parameter between any of the active treatment groups or the placebo group at any time point as assessed by the Investigator. All

hematology, coagulation and urinalysis values were assessed as normal or abnormal NCS.

This end-point reports the number of abnormal CS findings for hematology, coagulation or urinalysis parameters (none).

| End point type | Secondary |
|---|---|

End point timeframe:

Hematology, coagulation and urinalysis parameters were assessed at pre-specified visits from Visit 1 Screening to Visit 6 (Week 28).

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 44[107] | 45[108] | 46[109] | |
| Units: Number of abnormal CS findings | | | | |
| Abnormal CS findings | 0 | 0 | 0 | |

Notes:

[107] - At Week 28, 44 subjects remained in the study. For each specific analysis n may however vary.

[108] - At Week 28, 45 subjects remained in the study. For each specific analysis n may however vary.

[109] - At Week 28, 46 subjects remained in the study. For each specific analysis n may however vary.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Treatment compliance

| End point title | Treatment compliance |
|---|---|

End point description:

This end-point reports the IMP compliance (%), calculated as follows:

compliance=(number of delivered capsules − number of returned capsules)/number of delivered capsules

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

Compliance was calculated for subjects who had completed the whole treatment period.

| **End point values** | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 46 | 49 | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | 95 (± 10) | 96 (± 5) | 93 (± 10) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Absolute change from baseline in GSRS total score

| End point title | Absolute change from baseline in GSRS total score |
|---|---|

End point description:

The gastrointestinal symptom rating scale (GSRS) questionnaire contains 15 items in 5 dimensions (diarrhea syndrome, indigestion syndrome, constipation syndrome, abdominal pain syndrome and reflux syndrome) and uses a 7-graded Likert scale where 1 represents the most positive option and 7 the most negative one (no discomfort at all, minor discomfort, mild discomfort, moderate discomfort, moderately severe discomfort, severe discomfort, very severe discomfort).

This end-point reports the mean absolute change from baseline in GSRS total score at end of Week 2, end of Week 4, Week 7, End of Week 8, Week 14 and Week 26.

The data presented for this end-point was based on the full analysis set (FAS), i.e. all subjects who were randomised and received at least one dose of the IMP and who had at least one post-baseline assessment of efficacy data.

| End point type | Secondary |
|---|---|

End point timeframe:

The GSRS questionnaire was answered by the subjects at Visit 2 (Day 1, Baseline), end of Week 2 and 4, Visit 3 (Week 7), end of Week 8, Visit 4 (Week 14) and Visit 5 (Week 26).

| End point values | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 52[110] | 49[111] | 51[112] | |
| Units: number | | | | |
| arithmetic mean (standard deviation) | | | | |
| End of Week 2 | 0.6 (± 0.7) | 0.7 (± 0.6) | 0.3 (± 0.6) | |
| End of Week 4 | 0.7 (± 0.7) | 0.7 (± 0.5) | 0.3 (± 0.5) | |
| Week 7 | 0.9 (± 0.7) | 0.9 (± 0.7) | 0.3 (± 0.5) | |
| End of Week 8 | 0.8 (± 0.8) | 0.9 (± 0.7) | 0.4 (± 0.5) | |
| Week 14 | 0.8 (± 0.9) | 1.0 (± 0.7) | 0.3 (± 0.5) | |
| Week 26 | 0.6 (± 0.8) | 0.7 (± 0.7) | 0.1 (± 0.4) | |

Notes:

[110] - n=52 for Week 2
n=49 for Week 4
n=45 for Week 7
n=48 for Week 8
n=42 for Week 14 & 26
[111] - n=49 for Week 2, 4 & 8
n=41 for Week 7
n=45 for Week 14
n=42 for Week 26
[112] - n=51 for Week 2
n=52 for Week 4
n=45 for Week 7
n=49 for Week 8
n=48 for Week 14
n=47 for W 26

## Statistical analyses

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - End of Week 2 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as

independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0271 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - End of Week 2 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0033 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - End of Week 4 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 101 (the number 103 refers to End of Week 2).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0004 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - End of Week 4 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 101 (the number 100 refers to End of Week 2).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0005 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 103 refers to End of Week 2).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 7 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 86 (the number 100 refers to End of Week 2).

| | |
|---|---|
| Comparison groups | EMP16-02 - 150/50 v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 120/40 VS placebo - End of Week 8 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 97 (the number 103 refers to End of Week 2).

| | |
|---|---|
| Comparison groups | EMP16-02 - 120/40 v Placebo |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - End of Week 8 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 98 (the number 100 refers to End of Week 2).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0008 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 90 (the number 103 refers to End of Week 2).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0015 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 150/50 VS placebo - Week 14 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 93 (the number 100 refers to End of Week 2).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| Statistical analysis title | EMP16-02 - 120/40 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 89 (the number 103 refers to End of Week 2).

| Comparison groups | EMP16-02 - 120/40 v Placebo |
|---|---|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0017 |
| Method | ANCOVA |

| **Statistical analysis title** | EMP16-02 - 150/50 VS placebo - Week 26 |
|---|---|

Statistical analysis description:

The absolute change from baseline in total score were analyzed using ANCOVA, with treatment as independent variable and body weight at baseline as covariate.

The total number of subjects included in the analysis was 89 (the number 100 refers to End of Week 2).

| Comparison groups | EMP16-02 - 150/50 v Placebo |
|---|---|
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs (including serious AEs [SAEs]) were collected from the start of IMP administration until the end-of-study visit of each part.

Adverse event reporting additional description:

The grading of the severity of AEs followed the common terminology criteria for AEs (CTCAE) v5.0. AEs were assessed as unlikely, possibly or probably related to the IMP. GI symptoms were recorded using the GSRS questionnaire. Only symptoms assessed by the Investigator as severe were recorded as AEs unless the GI symptom led to an early withdrawal.

| Assessment type | Systematic |
|---|---|

### Dictionary used

| Dictionary name | MedDRA |
|---|---|
| Dictionary version | 23.0 |

### Reporting groups

| Reporting group title | EMP16-02 - 120/40 |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02 -120/40 (120 mg orlistat/40 mg acarbose).

| Reporting group title | EMP16-02 - 150/50 |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive EMP16-02-150/50 (150 mg orlistat/50 mg acarbose).

| Reporting group title | Placebo |
|---|---|

Reporting group description:

In this study patients were randomized in a 1:1:1 ratio to either of 2 doses of EMP16-02 or placebo. This arm (n=52) represents the group of patients who were randomized to receive placebo.

| Serious adverse events | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | EMP16-02 - 120/40 | EMP16-02 - 150/50 | Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 52 (61.54%) | 39 / 52 (75.00%) | 30 / 52 (57.69%) |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| Hypertension | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Surgical and medical procedures** | | | |
| Knee operation | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin neoplasm excision | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toe operation | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **General disorders and administration site conditions** | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Condition aggravated | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 3 / 52 (5.77%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Inflammation | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sensation of foreign body | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Reproductive system and breast disorders** | | | |
| Haematospermia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Menometrorrhagia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 2 / 52 (3.85%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| **Psychiatric disorders** | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 2 / 52 (3.85%) |
| occurrences (all) | 0 | 0 | 2 |
| Hallucination, auditory | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| Major depression | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Investigations** | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Injury, poisoning and procedural complications** | | | |

| | | | |
|---|---|---|---|
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 0 | 1 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Cardiac disorders** | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Nervous system disorders** | | | |
| Amnesia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 2 / 52 (3.85%) | 3 / 52 (5.77%) |
| occurrences (all) | 5 | 2 | 4 |
| Paresthesia | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Ear and labyrinth disorders** | | | |
| Otolithiasis | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| Vertigo positional | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Eye disorders** | | | |

| Blepharitis | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| | | | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| Gastrointestinal disorders | | | |
|---|---|---|---|
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| | | | |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| | | | |
| defecation urgency | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 2 / 52 (3.85%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 2 | 1 |
| | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 52 (15.38%) | 8 / 52 (15.38%) | 0 / 52 (0.00%) |
| occurrences (all) | 9 | 9 | 0 |
| | | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 0 | 1 |
| | | | |
| Encopresis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| **Flatulence** | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 3 / 52 (5.77%) | 1 / 52 (1.92%) |
| occurrences (all) | 4 | 4 | 1 |
| **Food poisoning** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Gastrointestinal motility disorder** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Gastroesophageal reflux disease** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 0 | 1 |
| **Lip swelling** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Mucous stools** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Nausea** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Toothache** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Skin and subcutaneous tissue disorders** | | | |
| **Alopecia** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Eczema** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| **Hyperhidrosis** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| **Petechiae** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Pruritus** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 1 | 1 |
| **Rash** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Urticaria** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Renal and urinary disorders** | | | |
| **Hypertonic bladder** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Musculoskeletal and connective tissue disorders** | | | |
| **Arthralgia** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 2 / 52 (3.85%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 3 | 1 |
| **Back pain** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 0 | 1 |
| **Joint swelling** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Musculoskeletal pain** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Myalgia** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Myositis** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Neck pain** | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Pain in extremity** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Plantar fasciitis** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| **Synovial cyst** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Tendonitis** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| **Infections and infestations** | | | |
| **COVID-19** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 6 / 52 (11.54%) | 2 / 52 (3.85%) |
| occurrences (all) | 0 | 6 | 2 |
| **Ear infection** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Fungal skin infection** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Gastroenteritis** | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| **Gastrointestinal infection** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Herpes zoster** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| **Influenza** | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 10 / 52 (19.23%) | 13 / 52 (25.00%) |
| occurrences (all) | 4 | 10 | 15 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 2 / 52 (3.85%) |
| occurrences (all) | 0 | 0 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 52 (1.92%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 1 | 1 |
| Food craving | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| Increased appetite | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?  Yes

| Date | Amendment |
|------|-----------|
| 17 November 2020 | Addition of a voluntary, long-term follow-up visit 6 months after completion of the 26-weeks treatment period with EMP16 02 for assessment of weight, HbA1c and blood pressure. Addition of trough plasma concentration measurements of acarbose at steady state. Administrative changes, clarifications and corrections of typos. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial?  No

### Limitations and caveats

 None reported