



Clinical trial results:

Blood Glucose Response After Oral Intake of Lactulose (Laevolac®) in Mildly Constipated Patients with Diabetes Mellitus Type 2

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-002359-14 |
| Trial protocol | AT |
| Global end of trial date | 08 March 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 10 June 2020 |
| First version publication date | 10 June 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | Lact-004-CP4 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03666546 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Fresenius Kabi Deutschland GmbH |
| Sponsor organisation address | Else-Kröner-Straße 1, Bad Homburg, Germany, 61346 |
| Public contact | Medical Affairs & Clinical Operations Parenteral Nutrition & Keto-Analogues, Fresenius Kabi Deutschland GmbH, trial-disclosure@fresenius-kabi.com |
| Scientific contact | Medical Affairs & Clinical Operations Parenteral Nutrition & Keto-Analogues, Fresenius Kabi Deutschland GmbH, trial-disclosure@fresenius-kabi.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 | 23 May 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 March 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 March 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to investigate whether lactulose, given orally as powder or liquid, increases blood glucose levels in patients with diabetes mellitus type 2. The dose of lactulose given in the trial is normally used for treatment of constipation.

Protection of trial subjects:

Subject protection was ensured by high medical and ethical standards in accordance with Declaration of Helsinki, Good Clinical Practice and applicable national and local laws and regulations. The signed informed consent was obtained from the patient prior to inclusion in the study.

Background therapy:

All study patients had non-insulin requiring diabetes mellitus type 2 and were treated with diet and oral antidiabetic drugs and/or Glucagon-like peptide(GLP)-1 receptor agonists. Diabetes mellitus treatment had to be stable, without any changes in diabetes mellitus related medication within the last 3 months. On days with study treatment, the intake of the antidiabetic medication in the morning was postponed until was postponed until breakfast after the test. Study products were consumed orally as single dose after overnight fast. Over a period of 180 minutes, when blood glucose levels were monitored in capillary blood, patients had to stay fasting and only water was served.

Evidence for comparator:

Water (placebo) was chosen as comparator to estimate normal physiologic variability of capillary blood glucose level over the Observation period of 180 minutes after intake of the study products. A dose of 30 g glucose (active comparator) was used as reference to evaluate the blood glucose level increase, this dose was chosen because it was considered as a comparable amount to the highest dose of Laevolac®.

| | |
|---|------------------|
| Actual start date of recruitment | 19 November 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Austria: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 13 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screened were non-insulin requiring patients with diabetes mellitus type 2, treated with diet and oral antidiabetics and/or GLP1 receptor agonists

- Age 18 - 75 years
- Glycosylated haemoglobin (HbA1c) ≤ 7.5 %
- No change in diabetes mellitus related medication within the last 3 months
- Mild functional constipation for the last 3 months

Period 1

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

Blinding implementation details:

The preparation of study products (blinding, reconstitution and labelling of drinking flasks) was done by unblinded staff by four-eyes principle. Test and control products were dissolved in 250 mL still water in non-transparent dark drinking flasks. The flasks had to bear the same blinded study specific labels which precluded unblinding by visual inspection. The flasks were provided to the blinded site personnel and Investigator to preserve the blind for Investigator and study patients.

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | No |
| Arm title | Laevolac® liquid 20 g |

Arm description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 17 received Laevolac® liquid 20 g as one of 4 different study treatments.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Laevolac® liquid |
| Investigational medicinal product code | |
| Other name | Lactulose |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Laevolac® liquid 20 g was dissolved in 250 mL still water. Solution was consumed orally as single dose after overnight fast within 5 minutes.

| | |
|------------------|-----------------------|
| Arm title | Laevolac® liquid 30 g |
|------------------|-----------------------|

Arm description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 15 received Laevolac® liquid 30 g as one of 4 different study treatments.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Laevolac® liquid |
| Investigational medicinal product code | |
| Other name | Lactulose |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Laevolac® liquid 30 g was dissolved in 250 mL still water. Solution was consumed orally as single dose

after overnight fast within 5 minutes.

| | |
|--|--------------------------|
| Arm title | Laevolac® crystals 20 g |
| Arm description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 20 g as one of 4 different study treatments. | |
| Arm type | Experimental |
| Investigational medicinal product name | Laevolac® crystals |
| Investigational medicinal product code | |
| Other name | Lactulose |
| Pharmaceutical forms | Powder for oral solution |
| Routes of administration | Oral use |
| Dosage and administration details: Laevolac® crystals 20 g was dissolved in 250 mL still water. Solution was consumed orally as single dose after overnight fast within 5 minutes. | |
| Arm title | Laevolac® crystals 30 g |
| Arm description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 30 g as one of 4 different study treatments. | |
| Arm type | Experimental |
| Investigational medicinal product name | Laevolac® crystals |
| Investigational medicinal product code | |
| Other name | Lactulose |
| Pharmaceutical forms | Powder for oral solution |
| Routes of administration | Oral use |
| Dosage and administration details: Laevolac® crystals 30 g was dissolved in 250 mL still water. Solution was consumed orally as single dose after overnight fast within 5 minutes. | |
| Arm title | Glucose 30 g |
| Arm description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Glucose 30 g as one of 4 different study treatments. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Glucose monohydrate |
| Investigational medicinal product code | |
| Other name | Glucose |
| Pharmaceutical forms | Powder for oral solution |
| Routes of administration | Oral use |
| Dosage and administration details: Glucose 30 g (Glucose monohydrate 33 g) was dissolved in 250 mL still water. Solution was consumed orally as single dose after overnight fast within 5 minutes. | |
| Arm title | Water |
| Arm description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Water as one of 4 different study treatments. | |
| Arm type | Placebo |

| | |
|--|-------------|
| Investigational medicinal product name | Still water |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral liquid |
| Routes of administration | Oral use |

Dosage and administration details:

250 mL still water was consumed orally as single dose after overnight fast within 5 minutes.

| Number of subjects in period 1 | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g |
|---------------------------------------|-----------------------|-----------------------|-------------------------|
| Started | 17 | 15 | 16 |
| Completed | 17 | 15 | 16 |

| Number of subjects in period 1 | Laevolac® crystals 30 g | Glucose 30 g | Water |
|---------------------------------------|-------------------------|--------------|-------|
| Started | 16 | 16 | 16 |
| Completed | 16 | 16 | 16 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Treatment Phase |
|-----------------------|-----------------|

Reporting group description:

The study was performed as 4-period cross-over with incomplete block design, stratified by gender. 24 patients were enrolled. Patients were randomized to one of 6 treatment sequences; each patient received 4 of the 6 different study products (6 arms).

| Reporting group values | Treatment Phase | Total | |
|---|-----------------|-------|--|
| Number of subjects | 24 | 24 | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 13 | 13 | |
| From 65-84 years | 11 | 11 | |
| 85 years and over | 0 | 0 | |
| Age continuous Units: years | | | |
| arithmetic mean | 62.2 | | |
| standard deviation | ± 7.61 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 8 | 8 | |
| Male | 16 | 16 | |

End points

End points reporting groups

| | |
|--|-------------------------|
| Reporting group title | Laevolac® liquid 20 g |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 17 received Laevolac® liquid 20 g as one of 4 different study treatments. | |
| Reporting group title | Laevolac® liquid 30 g |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 15 received Laevolac® liquid 30 g as one of 4 different study treatments. | |
| Reporting group title | Laevolac® crystals 20 g |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 20 g as one of 4 different study treatments. | |
| Reporting group title | Laevolac® crystals 30 g |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 30 g as one of 4 different study treatments. | |
| Reporting group title | Glucose 30 g |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Glucose 30 g as one of 4 different study treatments. | |
| Reporting group title | Water |
| Reporting group description: Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Water as one of 4 different study treatments. | |

Primary: Capillary blood glucose levels as baseline corrected AUC: AUCbaseline_c (0-180 min)

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|--|---|
| End point title | Capillary blood glucose levels as baseline corrected AUC: AUCbaseline_c (0-180 min) |
| End point description: Baseline corrected area under curve (AUC) of blood glucose concentrations from time 0 to 180 minutes after intake of the study products. (AUCbaseline_c is defined as AUC(0-180 min) - (baseline*180 min). | |
| End point type | Primary |
| End point timeframe: From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product. | |

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | -443.8 (± 1291.52) | -743.8 (± 1577.91) | -964.2 (± 1321.89) | -484.2 (± 1280.63) |

| End point values | Glucose 30 g | Water | | |
|--------------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | 8440 (± 2636.0) | -758.0 (± 1320.23) | | |

Statistical analyses

| Statistical analysis title | Mixed model arm 1 v 6 |
|---|-------------------------------|
| Comparison groups | Laevolac® liquid 20 g v Water |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 405.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -633.92 |
| upper limit | 1444.39 |

| Statistical analysis title | Mixed model arm 2 v 6 |
|---|-------------------------------|
| Comparison groups | Laevolac® liquid 30 g v Water |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 219.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -855.54 |
| upper limit | 1295.12 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 3 v 6 |
| Comparison groups | Laevolac® crystals 20 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | -21.5269 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1095.13 |
| upper limit | 1052.08 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 4 v 6 |
| Comparison groups | Laevolac® crystals 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 405.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -667.49 |
| upper limit | 1478.51 |

| | |
|---|--------------------------------------|
| Statistical analysis title | Mixed model arm 5 v 2 |
| Comparison groups | Glucose 30 g v Laevolac® liquid 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 9024.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7917.58 |
| upper limit | 10131 |

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | Mixed model arm 5 v 4 |
|-----------------------------------|-----------------------|

| | |
|---|--|
| Comparison groups | Glucose 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 8838.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7781.86 |
| upper limit | 9895.09 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 5 v 6 |
| Comparison groups | Glucose 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 9243.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8170.95 |
| upper limit | 10317 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 1 v 3 |
| Comparison groups | Laevolac® liquid 20 g v Laevolac® crystals 20 g |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 426.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -627.87 |
| upper limit | 1481.39 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Mixed model arm 2 v 4 |
| Comparison groups | Laevolac® liquid 30 g v Laevolac® crystals 30 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | -185.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1289.75 |
| upper limit | 918.31 |

Secondary: Maximum blood glucose concentration: Cmax

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|------------------------|--|
| End point title | Maximum blood glucose concentration: Cmax |
| End point description: | Maximum blood glucose concentration derived from the individual blood glucose concentration time curves from time 0 to 180 minutes after intake of the study products. |
| End point type | Secondary |
| End point timeframe: | From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product. |

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | 141.6 (± 16.71) | 149.2 (± 19.91) | 131.4 (± 17.88) | 139.5 (± 25.44) |

| End point values | Glucose 30 g | Water | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | 236.5 (± 29.95) | 136.6 (± 15.76) | | |

Statistical analyses

| | |
|----------------------------|-------------------------------|
| Statistical analysis title | Mixed model arm 1 v 6 |
| Comparison groups | Laevolac® liquid 20 g v Water |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 5.5231 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.164 |
| upper limit | 13.2102 |

| | |
|---|--------------------------------|
| Statistical analysis title | Mixed model arm 2 v 6 |
| Comparison groups | Laevolac® liquid 30 g v Water |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 11.321 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.3808 |
| upper limit | 19.2611 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 3 v 6 |
| Comparison groups | Laevolac® crystals 20 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 1.0074 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9024 |
| upper limit | 8.9172 |

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Mixed model arm 4 v 6 |
| Comparison groups | Laevolac® crystals 30 g v Water |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 5.8679 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.0297 |
| upper limit | 13.7655 |

| | |
|---|--------------------------------------|
| Statistical analysis title | Mixed model arm 5 v 2 |
| Comparison groups | Glucose 30 g v Laevolac® liquid 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 92.881 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 84.7739 |
| upper limit | 100.99 |

| | |
|---|--|
| Statistical analysis title | Mixed model arm 5 v 4 |
| Comparison groups | Glucose 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 98.3341 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 90.5138 |
| upper limit | 106.15 |

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | Mixed model arm 5 v 6 |
| Comparison groups | Glucose 30 g v Water |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 104.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 96.3025 |
| upper limit | 112.1 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 1 v 3 |
| Comparison groups | Laevolac® liquid 20 g v Laevolac® crystals 20 g |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 4.5157 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2607 |
| upper limit | 12.292 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 2 v 4 |
| Comparison groups | Laevolac® liquid 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least squares means |
| Point estimate | 5.4531 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6411 |
| upper limit | 13.5472 |

Secondary: Maximum increase of blood glucose concentration (Cmax minus baseline value): Max_increase

| | |
|-----------------|---|
| End point title | Maximum increase of blood glucose concentration (Cmax minus baseline value): Max_increase |
|-----------------|---|

End point description:

Maximum increase of blood glucose concentration (Cmax minus baseline value) derived from the individual blood glucose concentration time curves from time 0 to 180 minutes after intake of the study products.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product. | |

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | 12.62 (± 7.208) | 18.43 (± 10.321) | 7.688 (± 7.1969) | 12.81 (± 11.180) |

| End point values | Glucose 30 g | Water | | |
|--------------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | 110.9 (± 20.99) | 7.875 (± 6.9821) | | |

Statistical analyses

| Statistical analysis title | Mixed model arm 1 v 6 |
|---|-------------------------------|
| Comparison groups | Laevolac® liquid 20 g v Water |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 5.5231 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.164 |
| upper limit | 13.2102 |

| Statistical analysis title | Mixed model arm 2 v 6 |
|----------------------------|-------------------------------|
| Comparison groups | Laevolac® liquid 30 g v Water |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 11.321 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.3808 |
| upper limit | 19.2611 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 3 v 6 |
| Comparison groups | Laevolac® crystals 20 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 1.0074 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9024 |
| upper limit | 8.9172 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 4 v 6 |
| Comparison groups | Laevolac® crystals 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 5.8679 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.0297 |
| upper limit | 13.7655 |

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Mixed model arm 5 v 2 |
| Comparison groups | Laevolac® liquid 30 g v Glucose 30 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 92.881 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 84.7739 |
| upper limit | 100.99 |

| | |
|---|--|
| Statistical analysis title | Mixed model arm 5 v 4 |
| Comparison groups | Laevolac® crystals 30 g v Glucose 30 g |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 98.3341 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 90.5138 |
| upper limit | 106.15 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 5 v 6 |
| Comparison groups | Glucose 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 104.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 96.3025 |
| upper limit | 112.1 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Mixed model arm 1 v 3 |
| Comparison groups | Laevolac® liquid 20 g v Laevolac® crystals 20 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 4.5157 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2607 |
| upper limit | 12.292 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 2 v 4 |
| Comparison groups | Laevolac® liquid 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 5.4531 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6411 |
| upper limit | 13.5472 |

Secondary: Relative maximum increase of blood glucose concentration (Cmax / baseline value): Max_increase_rel

| | |
|-----------------|--|
| End point title | Relative maximum increase of blood glucose concentration (Cmax / baseline value): Max_increase_rel |
|-----------------|--|

End point description:

Relative maximum increase of blood glucose concentration (Cmax / baseline value) derived from the individual blood glucose concentration time curves from time 0 to 180 minutes after intake of the study products.

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

End point timeframe:

From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product.

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: mg/dL / mg/dL | | | | |
| arithmetic mean (standard deviation) | 1.101 (± 0.0610) | 1.145 (± 0.0847) | 1.063 (± 0.0593) | 1.108 (± 0.1005) |

| End point values | Glucose 30 g | Water | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: mg/dL / mg/dL | | | | |
| arithmetic mean (standard deviation) | 1.897 (± 0.1891) | 1.066 (± 0.0630) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum blood glucose concentration: Tmax

| | |
|-----------------|---|
| End point title | Time to reach maximum blood glucose concentration: Tmax |
|-----------------|---|

End point description:

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

End point timeframe:

From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product.

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|-------------------------------|------------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: minutes | | | | |
| median (full range (min-max)) | 30.00 (0.00 to 120.00) | 30.00 (0.00 to 60.00) | 30.00 (0.00 to 180.00) | 30.00 (0.00 to 60.00) |

| End point values | Glucose 30 g | Water | | |
|-------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: minutes | | | | |
| median (full range (min-max)) | 60.00 (45.00 to 60.00) | 22.50 (0.00 to 150.00) | | |

Statistical analyses

Secondary: Total AUC from 0 to 180 min for blood glucose concentration: AUC (0-180 min)

| | |
|-----------------|--|
| End point title | Total AUC from 0 to 180 min for blood glucose concentration: AUC (0-180 min) |
|-----------------|--|

End point description:

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

End point timeframe:

From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product.

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | 22766 (± 3092.3) | 22794 (± 3667.5) | 21311 (± 2806.7) | 22320 (± 4040.1) |

| End point values | Glucose 30 g | Water | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | 31053 (± 4807.7) | 22417 (± 2953.4) | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 1 v 6 |
| Comparison groups | Laevolac® liquid 20 g v Water |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 405.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -633.92 |
| upper limit | 1444.39 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 2 v 6 |
| Comparison groups | Laevolac® liquid 30 g v Water |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 219.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -855.54 |
| upper limit | 1295.12 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 3 v 6 |
| Comparison groups | Laevolac® crystals 20 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | -21.5269 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1095.13 |
| upper limit | 1052.08 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 4 v 6 |
| Comparison groups | Laevolac® crystals 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 405.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -667.49 |
| upper limit | 1478.51 |

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | Mixed model arm 5 v 2 |
|-----------------------------------|-----------------------|

| | |
|---|--------------------------------------|
| Comparison groups | Glucose 30 g v Laevolac® liquid 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 9024.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7917.58 |
| upper limit | 10131 |

| | |
|---|--|
| Statistical analysis title | Mixed model arm 5 v 4 |
| Comparison groups | Glucose 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 8838.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7781.86 |
| upper limit | 9895.09 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 5 v 6 |
| Comparison groups | Glucose 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 9243.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8170.95 |
| upper limit | 10317 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Mixed model arm 1 v 3 |
| Comparison groups | Laevolac® liquid 20 g v Laevolac® crystals 20 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 426.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -627.87 |
| upper limit | 1481.39 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 2 v 4 |
| Comparison groups | Laevolac® liquid 30 g v Laevolac® crystals 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | -185.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1289.75 |
| upper limit | 918.31 |

Secondary: Incremental AUC from 0 to 180 min for blood glucose concentration: iAUC (0-180 min)

| | |
|-----------------|---|
| End point title | Incremental AUC from 0 to 180 min for blood glucose concentration: iAUC (0-180 min) |
|-----------------|---|

End point description:

AUC above baseline levels for blood glucose concentration derived from the individual blood glucose concentration time curves from time 0 to 180 minutes after intake of the study products.

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

End point timeframe:

From 5 min before (blood glucose baseline value) to 180 min after ingestion of study product. Further blood glucose measurements 15, 30, 45, 60, 90, 150 and 180 min after ingestion of study product.

| End point values | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g | Laevolac® crystals 30 g |
|--------------------------------------|-----------------------|-----------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 16 |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | 619.7 (± 555.28) | 755.7 (± 673.84) | 296.3 (± 477.69) | 503.4 (± 499.11) |

| | | | | |
|--------------------------------------|-----------------|------------------|--|--|
| End point values | Glucose 30 g | Water | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: min*mg/dL | | | | |
| arithmetic mean (standard deviation) | 8677 (± 2384.1) | 350.7 (± 573.37) | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 1 v 6 |
| Comparison groups | Laevolac® liquid 20 g v Water |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 288.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -482.47 |
| upper limit | 1058.49 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 2 v 6 |
| Comparison groups | Laevolac® liquid 30 g v Water |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 425.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -369.73 |
| upper limit | 1220.7 |

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Mixed model arm 3 v 6 |
| Comparison groups | Laevolac® crystals 20 g v Water |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | -25.8996 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -813.73 |
| upper limit | 761.93 |

| | |
|---|---------------------------------|
| Statistical analysis title | Mixed model arm 4 v 6 |
| Comparison groups | Laevolac® crystals 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 165.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -619.67 |
| upper limit | 951.57 |

| | |
|---|--------------------------------------|
| Statistical analysis title | Mixed model arm 5 v 2 |
| Comparison groups | Laevolac® liquid 30 g v Glucose 30 g |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 7911.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7108.96 |
| upper limit | 8713.89 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Mixed model arm 5 v 4 |
| Comparison groups | Laevolac® crystals 30 g v Glucose 30 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 8170.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7386.6 |
| upper limit | 8955.33 |

| | |
|---|-------------------------------|
| Statistical analysis title | Mixed model arm 5 v 6 |
| Comparison groups | Glucose 30 g v Water |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 8336.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7550.95 |
| upper limit | 9122.88 |

| | |
|---|---|
| Statistical analysis title | Mixed model arm 1 v 3 |
| Comparison groups | Laevolac® liquid 20 g v Laevolac® crystals 20 g |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 872.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -461.79 |
| upper limit | 1089.61 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Mixed model arm 2 v 4 |
| Comparison groups | Laevolac® liquid 30 g v Laevolac® crystals 30 g |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference least square means |
| Point estimate | 259.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -542.14 |
| upper limit | 1061.22 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of AE reporting began with the fasting period the day before Screening Visit after Informed Consent (i.e. maximum 21 days before the first Treatment Visit) and ended 24 hours after the last of 4 Treatment Visits.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Laevolac® liquid 20 g |
|-----------------------|-----------------------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 17 received Laevolac® liquid 20 g as one of 4 different study treatments.

| | |
|-----------------------|-----------------------|
| Reporting group title | Laevolac® liquid 30 g |
|-----------------------|-----------------------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 15 received Laevolac® liquid 30 g as one of 4 different study treatments.

| | |
|-----------------------|-------------------------|
| Reporting group title | Laevolac® crystals 20 g |
|-----------------------|-------------------------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 20 g as one of 4 different study treatments.

| | |
|-----------------------|-------------------------|
| Reporting group title | Laevolac® crystals 30 g |
|-----------------------|-------------------------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Laevolac® crystals 30 g as one of 4 different study treatments.

| | |
|-----------------------|--------------|
| Reporting group title | Glucose 30 g |
|-----------------------|--------------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Glucose 30 g as one of 4 different study treatments.

| | |
|-----------------------|-------|
| Reporting group title | Water |
|-----------------------|-------|

Reporting group description:

Due to the 4-period cross-over design of the study, each patient was allocated to 4 arms, with a wash-out phase of 4 to 14 days to avoid carry-over effects. Of the 24 study patients, 16 received Water as one of 4 different study treatments.

| Serious adverse events | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g |
|---|-----------------------|-----------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| Serious adverse events | Laevolac® crystals 30 g | Glucose 30 g | Water |
|---|------------------------------------|---------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 16 (0.00%) | 0 / 16 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Laevolac® liquid 20 g | Laevolac® liquid 30 g | Laevolac® crystals 20 g |
|---|----------------------------------|----------------------------------|------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 17 (88.24%) | 15 / 15 (100.00%) | 12 / 16 (75.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 8 / 17 (47.06%) | 4 / 15 (26.67%) | 4 / 16 (25.00%) |
| occurrences (all) | 8 | 5 | 4 |
| Abdominal distension | | | |
| subjects affected / exposed | 6 / 17 (35.29%) | 7 / 15 (46.67%) | 5 / 16 (31.25%) |
| occurrences (all) | 11 | 8 | 5 |
| Abdominal pain | | | |

| | | | |
|--|------------------------|------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 3 / 17 (17.65%) 3 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 17 (29.41%) 5 | 9 / 15 (60.00%) 11 | 7 / 16 (43.75%) 8 |
| Dyspepsia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 15 (6.67%) 1 | 2 / 16 (12.50%) 2 |
| Eructation subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 15 (13.33%) 3 | 2 / 16 (12.50%) 2 |
| Flatulence subjects affected / exposed occurrences (all) | 11 / 17 (64.71%) 11 | 9 / 15 (60.00%) 9 | 8 / 16 (50.00%) 9 |
| Gastrointestinal sounds abnormal subjects affected / exposed occurrences (all) | 11 / 17 (64.71%) 14 | 13 / 15 (86.67%) 20 | 8 / 16 (50.00%) 10 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Regurgitation subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 15 (13.33%) 2 | 2 / 16 (12.50%) 2 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Psychiatric disorders Nervousness subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Tooth abscess subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |

| Non-serious adverse events | Laevolac® crystals 30 g | Glucose 30 g | Water |
|--|----------------------------|---------------------|---------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 14 / 16 (87.50%) | 9 / 16 (56.25%) | 7 / 16 (43.75%) |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 16 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 16 (6.25%) 1 | 0 / 16 (0.00%) 0 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Gastrointestinal disorders | | | |

| | | | |
|--|------------------------|----------------------|----------------------|
| Abdominal discomfort subjects affected / exposed occurrences (all) | 5 / 16 (31.25%) 5 | 2 / 16 (12.50%) 2 | 1 / 16 (6.25%) 1 |
| Abdominal distension subjects affected / exposed occurrences (all) | 7 / 16 (43.75%) 7 | 4 / 16 (25.00%) 4 | 3 / 16 (18.75%) 3 |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 4 | 0 / 16 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 16 (31.25%) 6 | 1 / 16 (6.25%) 1 | 1 / 16 (6.25%) 1 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 16 (12.50%) 2 | 0 / 16 (0.00%) 0 |
| Eructation subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 3 | 2 / 16 (12.50%) 2 | 2 / 16 (12.50%) 2 |
| Flatulence subjects affected / exposed occurrences (all) | 6 / 16 (37.50%) 7 | 4 / 16 (25.00%) 5 | 5 / 16 (31.25%) 5 |
| Gastrointestinal sounds abnormal subjects affected / exposed occurrences (all) | 11 / 16 (68.75%) 13 | 6 / 16 (37.50%) 6 | 4 / 16 (25.00%) 4 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 16 (12.50%) 2 | 0 / 16 (0.00%) 0 |
| Regurgitation subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 16 (12.50%) 2 | 1 / 16 (6.25%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Psychiatric disorders Nervousness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 16 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 1 / 16 (6.25%) 0 | 0 / 16 (0.00%) 0 0 / 16 (0.00%) 1 | 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 |
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Tooth abscess subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 1 / 16 (6.25%) 1 | 0 / 16 (0.00%) 0 1 / 16 (6.25%) 1 0 / 16 (0.00%) 0 | 1 / 16 (6.25%) 1 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported