



Clinical trial results:

A randomised, double-blind, placebo-controlled, parallel-group trial investigating the effect of 4 weeks bi-daily dosing of XEN-D0501 on blood glucose reduction as add-on to metformin in patients with diabetes type 2

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2018-001880-22 |
| Trial protocol | LT |
| Global end of trial date | 19 December 2019 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 14 January 2023 |
| First version publication date | 21 July 2022 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set The data set has been corrected and aligned with the final clinical study report. |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | PP-CT02 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05353686 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | PILA PHARMA AB |
| Sponsor organisation address | Västergatan 1 , Malmö, Sweden, 211 21 |
| Public contact | Dorte X. Gram, PILA PHARMA AB, +46 73903 6969, info@pilapharma.com |
| Scientific contact | Dorte X. Gram, PILA PHARMA AB, +46 73903 6969, info@pilapharma.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 June 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 December 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 December 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of four weeks of bi-daily dosing of XEN-D0501 (4 mg BID) as add-on to metformin on fasting blood glucose in patients with diabetes mellitus type 2

Protection of trial subjects:

None

Background therapy:

All subjects received metformin as background therapy.

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 February 2019 |
| 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 | Lithuania: 60 |
| Worldwide total number of subjects | 60 |
| EEA total number of subjects | 60 |

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) | 38 |
| From 65 to 84 years | 22 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 77 subjects gave informed consent and were screened. Of those, 60 subjects fulfilled the eligibility criteria and were randomised to treatment.

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-------------------|
| Number of subjects started | 77 ^[1] |
| Number of subjects completed | 60 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Consent withdrawn by subject: 1 |
| Reason: Number of subjects | Screen failures: 16 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification:

77 subject gave informed consent and 60 of those fulfilled the eligibility criteria and were randomized to treatment.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

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

Arm description:

1 tablet twice daily

| | |
|--|-------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Reference treatment (placebo) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1 oral tablet twice daily

| | |
|------------------|-----------|
| Arm title | XEN-D0501 |
|------------------|-----------|

Arm description:

1 tablet of 4 mg twice daily

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

| | |
|--|-----------|
| Investigational medicinal product name | XEN-D0501 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1 oral tablet of 4 mg twice daily | |

| Number of subjects in period 1 | Placebo | XEN-D0501 |
|--------------------------------|---------|-----------|
| Started | 31 | 29 |
| Completed | 31 | 29 |

Period 2

| | |
|------------------------------|---------------------------------------|
| Period 2 title | Treatment |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

1 tablet twice daily

| | |
|--|-------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Reference treatment (placebo) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1 oral tablet twice daily

| | |
|------------------|-----------|
| Arm title | XEN-D0501 |
|------------------|-----------|

Arm description:

1 tablet of 4 mg twice daily

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | XEN-D0501 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1 oral tablet of 4 mg twice daily

| Number of subjects in period 2 | Placebo | XEN-D0501 |
|---------------------------------------|---------|-----------|
| Started | 31 | 29 |
| Completed | 31 | 26 |
| Not completed | 0 | 3 |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | - | 1 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-----------|
| Reporting group title | Placebo |
| Reporting group description: 1 tablet twice daily | |
| Reporting group title | XEN-D0501 |
| Reporting group description: 1 tablet of 4 mg twice daily | |

| Reporting group values | Placebo | XEN-D0501 | Total |
|---|------------|------------|-------|
| Number of subjects | 31 | 29 | 60 |
| 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 Units: years | | | |
| geometric mean | 60.6 | 62.1 | |
| full range (min-max) | 29 to 84 | 49 to 77 | - |
| Gender categorical Units: Subjects | | | |
| Female | 21 | 16 | 37 |
| Male | 10 | 13 | 23 |
| Ethnic origin Units: Subjects | | | |
| White | 31 | 29 | 60 |
| Diabetes duration Units: Years | | | |
| geometric mean | 7.2 | 5.8 | |
| standard deviation | ± 5.9 | ± 3.6 | - |
| Height Units: cm | | | |
| geometric mean | 167.3 | 170.2 | |
| full range (min-max) | 149 to 185 | 146 to 187 | - |
| Weight Units: kg | | | |
| geometric mean | 92.3 | 99.2 | |
| full range (min-max) | 59 to 135 | 52 to 131 | - |
| BMI | | | |

| | | | |
|--|--------------------|--------------------|---|
| Units: mg/kg*2 geometric mean full range (min-max) | 33 23 to 46 | 34.3 19 to 46 | - |
| Waist circumference Units: cm geometric mean full range (min-max) | 110.1 87 to 149 | 114.2 79 to 137 | - |
| Hip circumference Units: cm geometric mean full range (min-max) | 114.1 95 to 139 | 116.5 87 to 141 | - |
| Waist-hip ratio Units: cm/cm geometric mean full range (min-max) | 1 0.8 to 1.1 | 1 0.8 to 1.1 | - |
| HbA1c Units: percent geometric mean standard deviation | 7.3 ± 0.92 | 7.5 ± 0.99 | - |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Placebo |
| Reporting group description: 1 tablet twice daily | |
| Reporting group title | XEN-D0501 |
| Reporting group description: 1 tablet of 4 mg twice daily | |
| Reporting group title | Placebo |
| Reporting group description: 1 tablet twice daily | |
| Reporting group title | XEN-D0501 |
| Reporting group description: 1 tablet of 4 mg twice daily | |
| Subject analysis set title | PP |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All participants in the study who completed the study and had no major protocol deviations. The PP population also excluded 3 participants with a minor protocol deviation, i.e., those who took the last study medication dose > 1 day (24 hours) before V4 | |
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All randomized participants | |

Primary: Fasting blood glucose after 4 weeks of treatment, PP population

| | |
|--|---|
| End point title | Fasting blood glucose after 4 weeks of treatment, PP population |
| End point description: Measured after four weeks of treatment (visit 4) and at baseline (visit 3) for the PP population | |
| End point type | Primary |
| End point timeframe: At 4 weeks after treatment (visit 4) | |

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: mmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Visit 4 | 7.868 (± 1.798) | 8.213 (± 2.034) | | |
| Change from baseline | -0.123 (± 1.114) | -0.272 (± 1.250) | | |
| Baseline (Visit 3) | 8.0 (± 1.9) | 8.5 (± 2.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Analysis of primary endpoint - visit 4 |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.5123 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.345 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.395 |
| upper limit | 0.705 |

| | |
|---|---|
| Statistical analysis title | Analysis of primary endpoint - change from BL |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.6452 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4986 |
| upper limit | 0.7978 |

Primary: Fasting blood glucose after 4 weeks of treatment, ITT population

| | |
|---|--|
| End point title | Fasting blood glucose after 4 weeks of treatment, ITT population |
| End point description: | |
| Measured after 4 weeks of treatment (visit 4) and at baseline (visit 3) from the ITT population | |
| End point type | Primary |
| End point timeframe: | |
| At 4 weeks after treatment (visit 4) | |

| End point values | Placebo | XEN-D0501 | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 29 | | |
| Units: mmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (visit 3) | 8.0 (± 1.9) | 8.6 (± 2.1) | | |
| Visit 4 | 7.9 (± 1.8) | 8.4 (± 2.1) | | |
| Change from baseline (visit 4- visit 3) | -0.1 (± 1.1) | -0.2 (± 1.2) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Analysis of primary endpoint - visit 4, ITT pop |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 60 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.3095 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.525 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5511 |
| upper limit | 0.5007 |

Secondary: Self-monitored blood glucose after 2 and 4 weeks of treatment

| | |
|----------------------------------|---|
| End point title | Self-monitored blood glucose after 2 and 4 weeks of treatment |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At 2 and 4 weeks after treatment | |

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: mmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Wake-up, 2 wks | 8.4 (± 2.5) | 8.7 (± 2.09) | | |
| Before breakfast, 2 wks | 8.8 (± 2.3) | 9.1 (± 2.0) | | |
| 2 hrs after breakfast, 2 wks | 9.4 (± 3.1) | 9.7 (± 3.2) | | |
| Before lunch, 2 wks | 7.3 (± 2.1) | 8.4 (± 2.7) | | |
| 2 hrs after lunch, 2 wks | 9.4 (± 2.4) | 9.2 (± 2.3) | | |
| 2 hrs after dinner, 2 wks | 8.6 (± 2.2) | 9.3 (± 2.2) | | |
| Bedtime, 2 hrs | 8.8 (± 3.0) | 9.0 (± 2.3) | | |
| Wake-up, 4 wks | 8.3 (± 1.9) | 8.6 (± 1.8) | | |
| Before breakfast, 4 wks | 8.4 (± 1.9) | 8.9 (± 1.9) | | |
| 2 hrs after breakfast, 4 wks | 9.0 (± 2.3) | 9.6 (± 3.3) | | |
| Before lunch, 4 wks | 7.4 (± 1.8) | 7.8 (± 2.7) | | |
| 2 hrs after lunch, 4 wks | 9.1 (± 3.0) | 8.9 (± 2.0) | | |
| 2 hrs after dinner, 4 wks | 9.3 (± 2.6) | 9.1 (± 2.2) | | |
| Bedtime, 4 wks | 8.8 (± 2.6) | 8.4 (± 2.5) | | |
| Before dinner, 2 wks | 8.2 (± 2.1) | 8.6 (± 2.6) | | |
| Before dinner, 4 wks | 8.2 (± 2.5) | 8.5 (± 2.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma HbA1c after 4 weeks of treatment

| | |
|--|---|
| End point title | Plasma HbA1c after 4 weeks of treatment |
| End point description: | |
| After 4 weeks of treatment (visit 4) and as change from baseline (visit 3) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks of treatment | |

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: percent | | | | |
| geometric mean (standard deviation) | | | | |
| Visit 4 | 7.2 (± 0.95) | 7.2 (± 0.93) | | |
| Change from baseline (visit 3) | -0.1 (± 0.33) | -0.2 (± 0.3) | | |
| Visit 3 | 7.3 (± 0.92) | 7.4 (± 0.98) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Glucose tolerance (OGTT) after 4 weeks of treatment

| | |
|-----------------|---|
| End point title | Glucose tolerance (OGTT) after 4 weeks of treatment |
|-----------------|---|

End point description:

Measured after 4 weeks of treatment (visit 4) and compared to baseline (-60 min)

Change of the changes from baseline represents the change between 120 and 0 min at visit 4 minus the change between 120 and 0 min at visit 3

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

End point timeframe:

At 4 weeks after treatment

| End point values | Placebo | XEN-D0501 | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: mmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| 4 weeks (visit 4), 120 min | 15.18 (\pm 3.17) | 13.42 (\pm 3.48) | | |
| 4 weeks (visit 4), change from baseline | 7.3 (\pm 2.9) | 5.2 (\pm 3.0) | | |
| Change of the changes | 0.69 (\pm 2.68) | -0.15 (\pm 2.4) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Plasma glucose at 120 min (V4 vs baseline -60 min) |
|----------------------------|--|

| | |
|-------------------|---------------------|
| Comparison groups | Placebo v XEN-D0501 |
|-------------------|---------------------|

| | |
|---|----|
| Number of subjects included in analysis | 54 |
|---|----|

| | |
|------------------------|----------|
| Analysis specification | Post-hoc |
|------------------------|----------|

| | |
|---------------|-------------|
| Analysis type | equivalence |
|---------------|-------------|

| | |
|---------|---------|
| P-value | = 0.013 |
|---------|---------|

| | |
|--------|-----------------|
| Method | t-test, 2-sided |
|--------|-----------------|

Secondary: Insulin secretion during an OGTT

| | |
|-----------------|----------------------------------|
| End point title | Insulin secretion during an OGTT |
|-----------------|----------------------------------|

End point description:

Measured after 4 weeks of treatment (visit 4) and compared to baseline (-60 min)

Change of the changes from baseline represents the change between 120 and 0 min at visit 4 minus the change between 120 and 0 min at visit 3

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

End point timeframe:

At 4 weeks after treatment

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: $\mu\text{U/mL}$ | | | | |
| geometric mean (standard deviation) | | | | |
| Actual 120 min (V4) | 57.2 (\pm 42.4) | 63.4 (\pm 42.3) | | |
| Change from baseline, 30 min | 20.1 (\pm 14.7) | 33.7 (\pm 22.9) | | |
| Change from baseline, 60 min | 33.5 (\pm 24.1) | 50.1 (\pm 34.9) | | |
| Change from baseline, 90 min | 43.3 (\pm 28.6) | 57.3 (\pm 43.2) | | |
| Change from baseline, 120 min | 44.3 (\pm 37.5) | 47.3 (\pm 35.8) | | |
| Change of the changes, 120 min | 2.9 (\pm 19.8) | 2.0 (\pm 31.1) | | |
| Actual 30 min (V4) | 33 (\pm 19.4) | 49.8 (\pm 30.1) | | |
| Actual 60 min (V4) | 46.3 (\pm 29.7) | 66.2 (\pm 42.4) | | |
| Actual 90 min (V4) | 56.5 (\pm 34.5) | 73.4 (\pm 49.4) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Insulin secretion at visit 4, 30 min (vs -60 min) |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.0178 |
| Method | t-test, 2-sided |

| | |
|---|---|
| Statistical analysis title | Insulin secretion at visit 4, 60 min (vs -60 min) |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.0429 |
| Method | t-test, 2-sided |

| | |
|-----------------------------------|---|
| Statistical analysis title | Insulin secretion at visit 4, 90 min (vs -60 min) |
| Comparison groups | Placebo v XEN-D0501 |

| | |
|---|-----------------|
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.1878 |
| Method | t-test, 2-sided |

| | |
|---|--|
| Statistical analysis title | Insulin secretion at visit 4, 120 min (vs -60 min) |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.7688 |
| Method | t-test, 2-sided |

Secondary: HOMA insulin resistance and beta cell function

| | |
|------------------------|--|
| End point title | HOMA insulin resistance and beta cell function |
| End point description: | Measured after 4 weeks of treatment (visit 4) and compared to baseline (visit 3) |
| End point type | Secondary |
| End point timeframe: | At 4 weeks after treatment |

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: pmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Insulin resistance, visit 4 | 4.5 (± 3.1) | 5.9 (± 4.5) | | |
| Insulin resistance, change from baseline visit 4 | -0.8 (± 2.1) | -1.0 (± 2.0) | | |
| Beta cell function, visit 4 | 67.1 (± 48.5) | 85.2 (± 80.8) | | |
| Beta cell function, change from baseline visit 4 | -9.9 (± 28.1) | 8.0 (± 78.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting insulin after 4 weeks of treatment

| | |
|-----------------|--|
| End point title | Fasting insulin after 4 weeks of treatment |
|-----------------|--|

| | |
|---|-----------|
| End point description: | |
| Measured 4 weeks after treatment (visit 4) and compared to baseline (visit 3) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks of treatment (visit 4) | |

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: µU/mL | | | | |
| geometric mean (standard deviation) | | | | |
| Insulin, visit 4 | 12.9 (± 8.0) | 16.1 (± 11.2) | | |
| Insulin, change from baseline | -2.3 (± 4.8) | -1.6 (± 4.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Body weight after 4 weeks of treatment

| | |
|---|--|
| End point title | Body weight after 4 weeks of treatment |
| End point description: | |
| Measured at baseline (visit 3) and after 4 weeks of treatment (visit 4) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks after treatment (visit 4) | |

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: Kg | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (visit 3) | 92.3 (± 20.4) | 103.4 (± 15.5) | | |
| Visit 4 | 91.8 (± 20.6) | 103.1 (± 15.3) | | |
| Change from baseline (visit 4 - visit 3) | -0.5 (± 1.4) | -0.3 (± 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Waist circumference

| | |
|---|---------------------|
| End point title | Waist circumference |
| End point description: | |
| Measured at baseline (visit 3) and after 4 weeks of treatment (visit 4) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks of treatment | |

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: cm | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (visit 3) | 109.7 (± 13.6) | 116.7 (± 11.8) | | |
| Visit 4 | 108.7 (± 13.4) | 116.5 (± 11.6) | | |
| Change from baseline (visit 4 - visit 3) | -0.9 (± 2.5) | -0.2 (± 1.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Waist-hip ratio

| | |
|---|-----------------|
| End point title | Waist-hip ratio |
| End point description: | |
| Measured at baseline (visit 3) and after 4 weeks of treatment (visit 4) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks after treatment (visit 4) | |

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: cm/cm | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (visit 3) | 1.0 (± 0.1) | 1.0 (± 0.1) | | |
| Visit 4 | 0.9 (± 0.1) | 1.0 (± 0.1) | | |
| Change from baseline (visit 4 - visit 3) | -0.006 (± 0.04) | -0.004 (± 0.02) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting blood lipids after 4 weeks of treatment

| | |
|-----------------|---|
| End point title | Fasting blood lipids after 4 weeks of treatment |
|-----------------|---|

End point description:

Measured after 4 weeks (visit 4) and as change from baseline (visit 4 - visit 3)

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

End point timeframe:

At 4 weeks of treatment (visit 4)

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: mmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| LDL, visit 4 | 3.2 (± 0.9) | 3.0 (± 1.17) | | |
| LDL, change from baseline | 0.05 (± 0.57) | 0.08 (± 0.55) | | |
| HDL, visit 4 | 1.3 (± 0.27) | 1.3 (± 0.35) | | |
| HDL, change from baseline | 0.007 (± 0.14) | 0.012 (± 0.15) | | |
| TAG, visit 4 | 2.3 (± 1.21) | 2.0 (± 0.7) | | |
| TAG, change from baseline | -0.051 (± 0.76) | -0.021 (± 0.48) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma CRP after 4 weeks of treatment

| | |
|-----------------|---------------------------------------|
| End point title | Plasma CRP after 4 weeks of treatment |
|-----------------|---------------------------------------|

End point description:

Measured after 4 weeks of treatment (visit 4) and as change from baseline (visit 4 - visit 3)

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

End point timeframe:

At 4 weeks of treatment (visit 4)

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: mg/L | | | | |
| geometric mean (standard deviation) | | | | |
| Visit 4 | 4.0 (± 4.7) | 5.1 (± 5.7) | | |
| Change from baseline | -1.33 (± 8.29) | 0.90 (± 5.61) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pro-BNP after 4 weeks of treatment

| | |
|-----------------|------------------------------------|
| End point title | Pro-BNP after 4 weeks of treatment |
|-----------------|------------------------------------|

End point description:

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

End point timeframe:

At 4 weeks of treatment (visit 4)

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 18 | | |
| Units: pg/mL | | | | |
| geometric mean (standard deviation) | | | | |
| Visit 4 | 475.8 (± 754.0) | 133.3 (± 85.0) | | |
| Change from baseline (visit 4 - visit 3) | 43.3 (± 213.1) | 13.1 (± 57.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Hyperthermia events

| | |
|-----------------|---------------------|
| End point title | Hyperthermia events |
|-----------------|---------------------|

End point description:

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

End point timeframe:

From start of treatment to follow-up, visit 5

| End point values | Placebo | XEN-D0501 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: Events | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Hypoglycemic events

| | |
|-----------------|---------------------|
| End point title | Hypoglycemic events |
|-----------------|---------------------|

End point description:

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

End point timeframe:

From start of treatment to follow-up (visit 5)

| End point values | Placebo | XEN-D0501 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: Events | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma glucagon after four weeks of bi-daily doses of XEN-D0501

| | |
|-----------------|---|
| End point title | Plasma glucagon after four weeks of bi-daily doses of XEN-D0501 |
|-----------------|---|

End point description:

Measured at baseline (visit 3) and after 4 weeks of treatment (visit 4)

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

End point timeframe:

After 4 weeks

| End point values | Placebo | XEN-D0501 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 28 | 22 | | |
| Units: pmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (visit 3) | 6.2 (± 4.5) | 5.4 (± 3.6) | | |
| Visit 4 | 6.4 (± 3.8) | 7.5 (± 5.5) | | |
| Change from baseline (visit 4 - visit 3) | 0.3 (± 3.7) | 3 (± 5.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of XEN-D0501 after four weeks of bi-daily dosing of XEN-D0501

| | |
|-----------------|--|
| End point title | Plasma concentration of XEN-D0501 after four weeks of bi-daily dosing of XEN-D0501 |
|-----------------|--|

End point description:

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

End point timeframe:

After 4 weeks

| End point values | XEN-D0501 | | | |
|--|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| Cmax | 66.2 (14.1 to 159) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

| | |
|-----------------|--------|
| End point title | Safety |
|-----------------|--------|

End point description:

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

End point timeframe:

From signing of informed content to end of trial participation

| End point values | Placebo | XEN-D0501 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 29 | | |
| Units: Events | | | | |
| Adverse events | 13 | 57 | | |
| SAEs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ANP after 4 weeks of treatment

| | |
|--|--------------------------------|
| End point title | ANP after 4 weeks of treatment |
| End point description: | |
| Measured 4 weeks after treatment and at baseline (visit 3) and as change from baseline | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 weeks | |

| End point values | Placebo | XEN-D0501 | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 23 | | |
| Units: pmol/L | | | | |
| geometric mean (standard deviation) | | | | |
| Visit 4 | 83.2 (± 65.3) | 58.9 (± 26.2) | | |
| Visit 3 | 78.2 (± 73.1) | 66.4 (± 24.5) | | |
| Change from baseline (visit 3) | 3.9 (± 14.1) | -7.5 (± 16.1) | | |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | ANP change from baseline |
| Comparison groups | Placebo v XEN-D0501 |
| Number of subjects included in analysis | 54 |
| Analysis specification | Post-hoc |
| Analysis type | equivalence |
| P-value | = 0.0097 |
| Method | t-test, 2-sided |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent to end of trial participation

Adverse event reporting additional description:

Adverse events are collected at each visit.

The Investigator asked the subjects about AEs by asking: "Have you experienced any problems since the last contact?"

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

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

Reporting group description: -

| | |
|-----------------------|-----------|
| Reporting group title | XEN-D0501 |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events | Placebo | XEN-D0501 | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 29 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Placebo | XEN-D0501 | |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 31 (29.03%) | 17 / 29 (58.62%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal polyp | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |

| | | | |
|--|---------------------|----------------------|--|
| Flushing subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 4 / 29 (13.79%) 4 | |
| Hypertension subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Surgical and medical procedures Skin neoplasm excision subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| General disorders and administration site conditions Feeling cold subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 3 / 29 (10.34%) 5 | |
| Feeling hot subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 3 / 29 (10.34%) 5 | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | 1 / 29 (3.45%) 1 | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 1 / 29 (3.45%) 1 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Investigations Body temperature increased subjects affected / exposed occurrences (all) | 3 / 31 (9.68%) 4 | 2 / 29 (6.90%) 2 | |
| Heart rate increased | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 3 | |
| Injury, poisoning and procedural complications Radius fracture subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Hypogeusia subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Taste disorder subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 2 / 29 (6.90%) 2 2 / 29 (6.90%) 3 1 / 29 (3.45%) 1 3 / 29 (10.34%) 3 3 / 29 (10.34%) 3 | |
| Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Tongue oedema subjects affected / exposed occurrences (all) Hypoaesthesia oral subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 1 / 29 (3.45%) 1 1 / 29 (3.45%) 1 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---------------------|----------------------|--|
| Hyperhidrosis subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 3 / 29 (10.34%) 4 | |
| Dermatitis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Renal and urinary disorders Polyuria subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Musculoskeletal and connective tissue disorders Carpal tunnel syndrome subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 2 | |
| Meniscus injury subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 29 (0.00%) 0 | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Metabolism and nutrition disorders Increased appetite subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 2 | 0 / 29 (0.00%) 0 | |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 29 (3.45%) 1 | |

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