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	• 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	33	34.3	
full range (min-max)	23 to 46	19 to 46	-
Waist circumference			
Units: cm			
geometric mean	110.1	114.2	
full range (min-max)	87 to 149	79 to 137	-
Hip circumference			
Units: cm			
geometric mean	114.1	116.5	
full range (min-max)	95 to 139	87 to 141	-
Waist-hip ratio			
Units: cm/cm			
geometric mean	1	1	
full range (min-max)	0.8 to 1.1	0.8 to 1.1	-
HbA1c			
Units: percent			
geometric mean	7.3	7.5	
standard deviation	± 0.92	± 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) fro 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 (± 3.17)	13.42 (± 3.48)		
4 weeks (visit 4), change from baseline	7.3 (± 2.9)	5.2 (± 3.0)		
Change of the changes	0.69 (± 2.68)	-0.15 (± 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: µU/mL				
geometric mean (standard deviation)				
Actual 120 min (V4)	57.2 (± 42.4)	63.4 (± 42.3)		
Change from baseline, 30 min	20.1 (± 14.7)	33.7 (± 22.9)		
Change from baseline, 60 min	33.5 (± 24.1)	50.1 (± 34.9)		
Change from baseline, 90 min	43.3 (± 28.6)	57.3 (± 43.2)		
Change from baseline, 120 min	44.3 (± 37.5)	47.3 (± 35.8)		
Change of the changes, 120 min	2.9 (± 19.8)	2.0 (± 31.1)		
Actual 30 min (V4)	33 (± 19.4)	49.8 (± 30.1)		
Actual 60 min (V4)	46.3 (± 29.7)	66.2 (± 42.4)		
Actual 90 min (V4)	56.5 (± 34.5)	73.4 (± 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	0 / 31 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Hot flush			
subjects affected / exposed	0 / 31 (0.00%)	4 / 29 (13.79%)	
occurrences (all)	0	4	
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Skin neoplasm excision			
subjects affected / exposed	0 / 31 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Feeling cold			
subjects affected / exposed	1 / 31 (3.23%)	3 / 29 (10.34%)	
occurrences (all)	1	5	
Feeling hot			
subjects affected / exposed	0 / 31 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	5	
Pyrexia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 31 (3.23%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Investigations			
Body temperature increased			
subjects affected / exposed	3 / 31 (9.68%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
Heart rate increased			

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

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