Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Study of the Neurokinin-1 Receptor Antagonist VPD-737 [Serlopitant] in Subjects with Prurigo Nodularis

Summary

EudraCT number	2013-005024-42
Trial protocol	DE IE PL
Global end of trial date	10 June 2016

Results information

Result version number	v1 (current)
This version publication date	30 July 2020
First version publication date	30 July 2020

Trial information

Trial identification

Sponsor protocol code	TCP-102

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Menlo Therapeutics Inc. (formerly Tigercat Pharma, Inc.)
Sponsor organisation address	4085 Campbell Avenue, Suite 200, Menlo Park, CA, United States, 94025
Public contact	Iain Stuart, PhD, Menlo Therapeutics, Inc., 1- 800-775-7936, Iain.Stuart@foamix.com
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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	31 August 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were to evaluate the efficacy and safety of Serlopitant 5 mg tablets and placebo taken orally once daily for 8 weeks for the treatment of prurigo nodularis (PN).

Protection of trial subjects:

The protocol, proposed informed consent form(s), and other information for subjects was reviewed and approved by central and local Ethics Committees (ECs) before the start of the trial, in compliance with local regulations. This study was conducted in compliance with the protocol and the applicable laws and regulatory requirements of Germany in which the study was conducted. The study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki and amendments and the International Council on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines. The investigator explained to each subject the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved, and any discomfort it might entail. Each subject was informed that participation in the study was voluntary, that he/she could withdraw from the study at any time, and that withdrawal of consent would not affect his/her subsequent medical treatment or relationship with the treating physician. No subject could enter the study before informed consent had been obtained from him/her, or his/her legally authorized representative.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 2014
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	Germany: 127
Worldwide total number of subjects	127
EEA total number of subjects	127

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)	88
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects were randomized at 15 sites in Germany.
Of the 128 subjects who were randomized, 127 received study drug.

Pre-assignment

Screening details:

This study consisted of a screening period of up to 4 weeks. All the assessments were done at screening as per the schedule of assessment.
One subject was randomized to Serlopitant but, due to an exacerbation of pruritus, received systemic cyclosporine treatment that was an exclusion criterion and therefore the subject never received study drug.

Period 1

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

Blinding implementation details:

This was as a double-blind study with the treatment assignment concealed from the subjects, the investigator(s) and their staff, and the clinical research team. The placebo was formulated to be indistinguishable from the active study product. Study materials were packaged and issued in a manner designed to maintain the blind for subjects and all study personnel involved in the direction and execution of study procedures, study assessments, and collection of data.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Randomized subjects took matching placebo tablets for oral administration as 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.

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

Dosage and administration details:

Matching placebo tablets for oral administration were taken orally as 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime.

Arm title	Serlopitant

Arm description:

Randomized subjects took Serlopitant 5 mg tablets for oral administration at a loading dose of 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Serlopitant
Investigational medicinal product code	VPD-737
Other name	Neurokinin-1 Receptor Antagonist VPD-737
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Serlopitant 5 mg tablets for oral administration were taken orally as a loading dose of 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime.

Number of subjects in period 1	Placebo	Serlopitant
Started	63	64
Completed	48	57
Not completed	15	7
Consent withdrawn by subject	8	4
Other	1	-
Adverse Event or Serious Adverse Event	6	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Randomized subjects took matching placebo tablets for oral administration as 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	
Reporting group title	Serlopitant
Reporting group description:	
Randomized subjects took Serlopitant 5 mg tablets for oral administration at a loading dose of 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	

Reporting group values	Placebo	Serlopitant	Total
Number of subjects	63	64	127
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			
arithmetic mean	58.1	57.1	
standard deviation	± 11.14	± 12.00	-
Gender categorical			
Units: Subjects			
Female	36	31	67
Male	27	33	60

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Randomized subjects took matching placebo tablets for oral administration as 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	
Reporting group title	Serlopitant
Reporting group description:	
Randomized subjects took Serlopitant 5 mg tablets for oral administration at a loading dose of 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	

Primary: Average Visual Analog Scale (VAS)

End point title	Average Visual Analog Scale (VAS)
End point description:	
At study visits, subjects recorded a mark for pruritus severity on a 10-cm horizontal line. This thermometer-type scale was marked with ratings of "no itch" (0 cm) and worst imaginable itch" (10 cm). Average VAS (average itch over the past 24 hours) was recorded. n= number of subjects analyzed	
End point type	Primary
End point timeframe:	
At Baseline, Weeks 2, 4, and 8	

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 63, 64)	7.92 (± 1.630)	7.88 (± 1.311)		
Week 2 (n = 61, 63)	7.01 (± 2.187)	6.06 (± 2.236)		
Week 4 (n = 54, 64)	6.32 (± 2.403)	5.41 (± 2.719)		
Week 8 (n = 46, 57)	5.56 (± 2.630)	4.21 (± 2.746)		

Statistical analyses

Statistical analysis title	Week 2
Statistical analysis description:	
Statistics for Repeated Measures of Change From Baseline	
Comparison groups	Placebo v Serlopitant

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0111
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Week 4
Statistical analysis description:	
Repeated Measures of Change from Baseline	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0248
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	Week 8
Statistical analysis description:	
Repeated Measures of Change from Baseline	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.47

Secondary: Verbal Rating Scale (VRS) - pruritus

End point title	Verbal Rating Scale (VRS) - pruritus

End point description:

At study visits, subjects used the VRS to rate their skin sensations (pruritus, burning, and stinging) using a 5-point scale (0 = not present; 1 = mild present; 2 = moderately present; 3 = severely present; and 4 = very severely present).

End point type	Secondary

End point timeframe:

At Baseline and Week 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Baseline (n=62,64) Mild Present	2	0		
Baseline (n=62,64) Moderately Present	18	17		
Baseline (n=62,64) Severely Present	20	32		
Baseline (n=62,64) Very Severely Present	22	15		
Week 8 (n=45, 57) Not Present	2	4		
Week 8 (n=45, 57) Mild Present	11	27		
Week 8 (n=45, 57) Moderately Present	18	17		
Week 8 (n=45, 57) Severely Present	9	7		
Week 8 (n=45, 57) Very Severely Present	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Verbal Rating Scale (VRS) - Burning

End point title	Verbal Rating Scale (VRS) - Burning

End point description:

At study visits, subjects used the VRS to rate their skin sensations (pruritus, burning, and stinging) using a 5-point scale (0 = not present; 1 = mild present; 2 = moderately present; 3 = severely present; and 4 = very severely present).

End point type	Secondary

End point timeframe:

At Baseline and Week 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Baseline (n=62,64) Not Present	14	21		
Baseline (n=62,64) Mild Present	8	5		
Baseline (n=62,64) Moderately Present	13	21		
Baseline (n=62,64) Severely Present	18	12		
Baseline (n=62,64) Very Severely Present	9	5		
Week 8 (n=43, 56) Not Present	11	31		
Week 8 (n=43, 56) Mild Present	9	10		
Week 8 (n=43, 56) Moderately Present	15	8		
Week 8 (n=43, 56) Severely Present	5	6		
Week 8 (n=43, 56) Very Severely Present	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Verbal Rating Scale (VRS) - Stinging

End point title	Verbal Rating Scale (VRS) - Stinging

End point description:

At study visits, subjects used the VRS to rate their skin sensations (pruritus, burning, and stinging) using a 5-point scale (0 = not present; 1 = mild present; 2 = moderately present; 3 = severely present; and 4 = very severely present).

End point type	Secondary

End point timeframe:

At Baseline and Week 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Baseline (n=62,64) Not Present	26	21		
Baseline (n=62,64) Mild Present	8	14		
Baseline (n=62,64) Moderately Present	11	16		

Baseline (n=62,64) Severely Present	9	10		
Baseline (n=62,64) Very Severely Present	8	3		
Week 8 (n=43, 54) Not Present	18	30		
Week 8 (n=43, 54) Mild Present	8	12		
Week 8 (n=43, 54) Moderately Present	10	7		
Week 8 (n=43, 54) Severely Present	4	4		
Week 8 (n=43, 54) Very Severely Present	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Worst Visual Analog Scale (VAS)

End point title	Worst Visual Analog Scale (VAS)

End point description:

At study visits, subjects recorded a mark for pruritus severity on a 10-cm horizontal line. This thermometer-type scale was marked with ratings of "no itch" (0 cm) and worst imaginable itch" (10 cm). Worst VAS (worst itch over the past 24 hours) was recorded.

End point type	Secondary

End point timeframe:

At Baseline, Weeks 2, 4, and 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n=63, 64)	8.75 (± 1.316)	8.43 (± 1.190)		
Week 2 (n=61, 63)	7.92 (± 1.733)	6.85 (± 2.157)		
Week 4 (n= 54, 64)	7.46 (± 2.285)	6.19 (± 2.690)		
Week 8 (n= 46, 57)	6.73 (± 2.591)	4.82 (± 2.729)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Assessment (PGA)

End point title	Patient Global Assessment (PGA)

End point description:

The PGA included a global question and dynamic sub-questions:
(1) Did the pruritus improve during the treatment period (yes/no)
(2) If yes, for how long (some minutes/some hours/some days)
(3) If yes relieved, to what extent
o 1%-30% (no or weak improvement)

o 31%-50% (moderate improvement)
o 51%-70% (good improvement)
o 71%-100% (very good improvement)
(4) Can you say it [the percentage improvement] exactly (___%).

End point type	Secondary
End point timeframe:	
At Weeks 2, 4, and 8	

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Percentage of Subjects				
number (not applicable)				
Week 2	37.7	58.7		
Week 4	53.7	67.2		
Week 8	54.3	82.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Numeric Rating Scale (NRS)

End point title	Numeric Rating Scale (NRS)

End point description:

Numeric Rating Scale: Using the patient diary, subjects rated the following using an 11-point NRS (0 = no itching; to 10 = worst itch imaginable):
(1) average itching over the past 24 hours (Average NRS).

End point type	Secondary
End point timeframe:	
At Baseline, Weeks 2, 4, and 8	

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n=48, 48)	7.65 (± 1.669)	7.60 (± 1.455)		
Week 2 (n=58,62)	6.23 (± 2.043)	5.50 (± 1.944)		
Week 4 (n=52,62)	5.80 (± 2.133)	4.91 (± 2.158)		
Week 8 (n=46,54)	5.11 (± 2.320)	4.02 (± 2.190)		

Statistical analyses

Statistical analysis title	Week 2
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0

Statistical analysis title	Week 4
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.1

Statistical analysis title	Week 8
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0175 [1]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.2

Notes:

[1] - p-value assume equal variance

Secondary: Dermatology Life Quality Index (DLQI)

End point title	Dermatology Life Quality Index (DLQI)

End point description:

At each visit, subjects completed a DLQI questionnaire. The DLQI is a validated questionnaire consisting of 10 questions relating to the degree to which the subject's skin condition affected his/her daily activities.

End point type	Secondary

End point timeframe:

At Baseline, Weeks 2, 4, and 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n=61,61)	14.9 (± 7.03)	13.7 (± 6.76)		
Week 2 (n=57,62)	12.4 (± 6.94)	11.6 (± 6.20)		
Week 4 (n=51,62)	11.6 (± 6.56)	11.4 (± 6.80)		
Week 8 (n=44,55)	11.3 (± 6.83)	10.6 (± 7.31)		

Statistical analyses

Statistical analysis title	Week 2

Statistical analysis description:

Observed results

Comparison groups	Placebo v Serlopitant

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.6

Statistical analysis title	Week 4
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	2.3

Statistical analysis title	Week 8
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	2.1

Secondary: Pruritus-specific Quality of Life (ItchyQoL)	
End point title	Pruritus-specific Quality of Life (ItchyQoL)

End point description:

At each visit, subjects completed an ItchyQoL questionnaire. The ItchyQoL is a validated questionnaire consisting of 22 questions based on the concerns and issues pertinent to patients with pruritus.

End point type	Secondary

End point timeframe:

At Baseline, Weeks 2, 4, and 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n=63,64)	3.68 (± 0.737)	3.52 (± 0.679)		
Week 2 (n=61,63)	3.50 (± 0.795)	3.36 (± 0.670)		
Week 4 (n=54,64)	3.36 (± 0.863)	3.26 (± 0.730)		
Week 8 (n=46,57)	3.33 (± 0.876)	3.09 (± 0.904)		

Statistical analyses

Statistical analysis title	Week 2
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.1

Statistical analysis title	Week 4
Statistical analysis description:	
Observed results)	
Comparison groups	Placebo v Serlopitant

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2

Statistical analysis title	Week 8
Statistical analysis description:	
Observed results	
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.1

Secondary: Patient Benefit Index, Version for Patients with Pruritus (PBI-P)

End point title	Patient Benefit Index, Version for Patients with Pruritus (PBI-P)

End point description:

At Visits 2 and 5 (or Early termination) only, subjects completed the standardized and validated PBI-P questionnaire. Prior to treatment, the first page of the questionnaire, the Patient Needs Questionnaire (PNQ), was administered to determine how different benefits of therapy were relevant for the individual subject. After treatment, using the Patient Benefit Questionnaire (PBQ), subjects were asked to evaluate the extent to which the benefits they indicated were important to them were, in fact, realized. From all the items taken together, a weighted total benefit value was calculated, which represented the patient-relevant therapy benefits.

End point type	Secondary

End point timeframe:

At Week 8 / End of Treatment

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	63		
Units: Unit on a scale				
arithmetic mean (standard deviation)	0.81 (± 0.984)	1.16 (± 1.095)		

Statistical analyses

Statistical analysis title	Week 8 / End of Treatment
Comparison groups	Placebo v Serlopitant
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0625 [2]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.72

Notes:

[2] - p-value assume equal variance.

Secondary: Investigator Global Assessment (IGA)

End point title	Investigator Global Assessment (IGA)

End point description:

Using the IGA, physicians rated change in PN lesions (if any) from +5 (“markedly improved”) to -5 (“markedly worse”).

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	57		
Units: Subjects				
number (not applicable)				
Markedly Improved	0	4		
Largely Improved	2	3		
Moderately To Largely Improved	4	3		
Moderately Improved	4	11		
Mildly Improved	9	17		
Baseline	14	7		

Mildly Worse	8	5		
Moderately Worse	4	4		
Moderately To Largely Worse	1	1		
Largely Worse	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Prurigo Activity Score (PAS)

End point title	Prurigo Activity Score (PAS)

End point description:

Using the PAS, physicians described, localized, counted, and measured PN lesions. The PAS was assessed at Visit 2 (Baseline), 3 (Week 2), 4 (Week 4), and 5 (Week 8) (or at Early termination). The 7 items were:
1) Type of PN lesion
a. Which efflorescences do you see? (6 possible responses)
b. Which type of prurigo is predominant? (6 possible responses)
2) Number of PN lesions (0, 1-19, 20-100, > 100)
3) Distribution (disseminated, localized, neither)
4) Affected areas (14 possible responses)
5) Lesions in the representative area (continuous variable) and the location of this area.
6) Lesion size (elevation, longitudinal, crosswise)
a. Biggest prurigo lesion
b. Representative prurigo lesion
7) Activity Stage (Stage 0-4: 0 = 0%, 1 = 1-25%, 2 = 26-50%, 3 = 51-75%, 4 = > 75%)
a. Prurigo lesions with excoriations/crusts
b. Healed prurigo lesions

PAS activity stage (prurigo lesions with excoriations/crusts) is presented in the below table.

End point type	Secondary

End point timeframe:

At Day 1 and Week 8

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Day 1 (n=63,64) 1 - 25 %	7	5		
Day 1 (n=63,64) 26 - 50 %	18	19		
Day 1 (n=63,64) 51 - 75 %	17	19		
Day 1 (n=63,64) >75 %	21	21		
Week 8 (n=47,57) 0 %	0	4		
Week 8 (n=47,57) 1 - 25 %	11	15		
Week 8 (n=47,57) 26 - 50 %	12	12		
Week 8 (n=47,57) 51 - 75 %	11	11		
Week 8 (n=47,57) >75 %	13	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Rescue medication usage

End point title	Rescue medication usage

End point description:

Rescue medications included cetirizine hydrochloride, desloratadine, levocetirizine, and loratadine.

End point type	Secondary

End point timeframe:

8 Weeks

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Pre-treatment Rescue Medication Used	15	17		
Used Rescue Medication	12	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events (AEs)

End point title	Number of subjects with adverse events (AEs)

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE (also referred to as an adverse experience) could be any unfavorable and unintended sign (eg, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, without any judgment about causality.

End point type	Secondary

End point timeframe:

From the time of informed consent (Screening) until the last study visit (follow-up phone call, Week 10)

End point values	Placebo	Serlopitant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: Subjects				
number (not applicable)				
Adverse events (AEs)	91	102		
Subjects with AEs	39	46		
Treatment-emergent adverse events (TEAEs)	91	102		
Subjects with TEAEs	39	46		
Subjects with TEAEs leading to discontinuation	6	3		
Subjects with TEAEs related to study drug	22	31		
Subjects with TEAEs by maximum severity, Mild	14	18		
Subjects with TEAEs by maximum severity, Moderate	22	22		
Subjects with TEAEs by maximum severity, Severe	3	6		
Subjects with serious TEAEs	2	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the time of informed consent (Screening) until the last study visit (follow-up phone call, Week 10).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Randomized subjects took matching placebo tablets for oral administration as 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	
Reporting group title	Serlopitant
Reporting group description:	
Randomized subjects took Serlopitant 5 mg tablets for oral administration at a loading dose of 3 tablets at baseline (Day 1) followed by 1 tablet every day at bedtime for 8 weeks.	

Serious adverse events	Placebo	Serlopitant	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 63 (3.17%)	3 / 64 (4.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic elastosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodermatitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Serlopitant	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 63 (31.75%)	31 / 64 (48.44%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 63 (1.59%)	4 / 64 (6.25%)	
occurrences (all)	1	4	
Headache			

subjects affected / exposed	4 / 63 (6.35%)	4 / 64 (6.25%)	
occurrences (all)	4	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 63 (6.35%)	6 / 64 (9.38%)	
occurrences (all)	4	6	
Oedema peripheral			
subjects affected / exposed	0 / 63 (0.00%)	4 / 64 (6.25%)	
occurrences (all)	0	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 63 (4.76%)	7 / 64 (10.94%)	
occurrences (all)	3	7	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 63 (11.11%)	3 / 64 (4.69%)	
occurrences (all)	7	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 63 (3.17%)	11 / 64 (17.19%)	
occurrences (all)	3	11	
Urinary tract infection			
subjects affected / exposed	4 / 63 (6.35%)	0 / 64 (0.00%)	
occurrences (all)	4	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2014	Subjects were first screened under Version 3.0 of the protocol (26 May 2014). Protocol Version 4.0 specified that efficacy analysis would be on the intent-to-treat (ITT) population.
19 September 2014	Protocol Version 5.0 Shortened the washout periods to 2 weeks for systemic prior therapies, 1 week for topical therapies, and 5 days for antihistamines. The additional review according to the Common Terminology Criteria for Adverse Events (CTCAE) of AEs previously classified as moderate toxicity or higher was deleted as those criteria are specified for cancer indications. As fluconazole was classified as a strong CYP3A4 inhibitor in the exclusion criteria, it was deleted in the section describing co-administration of weak and moderate CYP3A4 inhibitors.
16 April 2015	Protocol Version 6.0 The sample size, which was originally based on clinical judgment, was revised based on statistical estimates obtained on data from a recently completed study in pruritus. The total sample size was doubled to detect a statistically significant difference between treatment groups. Accordingly, the planned number of trial sites was increased and the estimated trial period was extended. The shelf-life extension and subsequent re-labelling of the study drug were added.
16 June 2015	Protocol Version 7.0 Originally, subjects who were at least 18 and no more than 75 years of age at screening were eligible for study entry. The maximum age was increased to no more than 80 years.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported