Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety, and Tolerability of Serlopitant for the Treatment of Pruritus in Adults With Prurigo Nodularis

Summary

EudraCT number	2017-004210-25
Trial protocol	DE AT PL
Global end of trial date	06 February 2020

Results information

Result version number	v1 (current)
This version publication date	21 January 2021
First version publication date	21 January 2021

Trial information

Trial identification

Sponsor protocol code	MTI-106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03677401
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Menlo Therapeutics Inc.
Sponsor organisation address	200 Cardinal Way, 2nd Floor, Redwood City, CA, United States, 94063
Public contact	Chief Scientific Officer, Menlo Therapeutics Inc., 1-800 775-7936, Iain.Stuart@foamix.com
Scientific contact	Chief Scientific Officer, Menlo Therapeutics Inc., 1-800 775-7936, Iain.Stuart@foamix.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	22 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2020
Global end of trial reached?	Yes
Global end of trial date	06 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to assess the efficacy of serlopitant for the treatment of pruritus in adults with prurigo nodularis (PN), and to assess the safety and tolerability of repeated oral doses of serlopitant in adults with PN.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Note for Guidance on Good Clinical Practice (GCP) (CPMP/ICH/135/95) and with applicable local requirements. Prior to the performance of any study-specific procedure, written informed consent was obtained from each subject. The subject was informed about the nature and purpose of the study, as well as of its risks and benefits. It was explained that the subject could withdraw from the study at any time and for any reason, and that this would not have any effect on his/her potential future medical care. Representative written information given to the subject and a sample of the Independent Ethics Committee/Institutional Review Board-approved consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 August 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	European Union: 295
Worldwide total number of subjects	295
EEA total number of subjects	0

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)	196
From 65 to 84 years	97
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted from 29 August 2018 to 06 February 2020.

Pre-assignment

Screening details:

During the screening period (4 weeks), all subjects were evaluated for eligibility and chronic pruritic conditions frequently associated with PN. Subjects were to complete an electronic diary (eDiary) at the Screening visit.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Randomized subjects received daily oral doses of placebo following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10-week treatment period.

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:

Subjects were randomized to receive once-daily oral doses of placebo for 10 weeks.

Arm title	Serlopitant 5 mg

Arm description:

Randomized subjects received daily oral doses of serlopitant 5 mg following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10- week treatment period.

Arm type	Experimental
Investigational medicinal product name	Selopitant 5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were randomized to receive once-daily oral doses of serlopitant 5 mg for 10 weeks.

Number of subjects in period 1	Placebo	Serlopitant 5 mg
Started	148	147
Completed	138	129
Not completed	10	18
Consent withdrawn by subject	2	2
Adverse event, non-fatal	4	14
Reason unspecified	1	-
Sponsor decision	-	1
Lack of efficacy	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Randomized subjects received daily oral doses of placebo following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10-week treatment period.	
Reporting group title	Serlopitant 5 mg
Reporting group description:	
Randomized subjects received daily oral doses of serlopitant 5 mg following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10- week treatment period.	

Reporting group values	Placebo	Serlopitant 5 mg	Total
Number of subjects	148	147	295
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	58.5	57.5	
standard deviation	± 12.97	± 15.33	-
Gender categorical Units: Subjects			
Female	94	98	192
Male	54	49	103
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	0	2
White	145	145	290
More than one race	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Randomized subjects received daily oral doses of placebo following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10-week treatment period.	
Reporting group title	Serlopitant 5 mg
Reporting group description:	
Randomized subjects received daily oral doses of serlopitant 5 mg following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10- week treatment period.	

Primary: Percent of Subjects With Worst Itch Numeric Rating Scale (WINRS) 4-point Responder Rate at Week 10

End point title	Percent of Subjects With Worst Itch Numeric Rating Scale (WINRS) 4-point Responder Rate at Week 10
End point description:	
During the study, WI-NRS assessments were reported by the subject via eDiary once daily from screening/mid-screening visit through the follow-up visit. The Itch NRS is a validated, self reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11- point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity. Subjects were considered responders if they had at least a 4-point reduction from Baseline in weekly average WI-NRS at Week 10.	
End point type	Primary
End point timeframe:	
At Week 10	

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Percentage of subjects				
number (not applicable)				
Success	18.95	25.90		
Failure	81.05	74.10		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
At Week 10	
Comparison groups	Placebo v Serlopitant 5 mg

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.158
Method	Cochran-Mantel-Haenszel

Notes:

[1] - P-value from a Cochran-Mantel- Haenszel (CMH) test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Secondary: Percent of Subjects With WI-NRS 4-point Responder Rate at Week 4

End point title	Percent of Subjects With WI-NRS 4-point Responder Rate at Week 4

End point description:

During the study, WI-NRS assessments were reported by the subject via eDiary once daily from screening/mid-screening visit through the follow-up visit. The Itch NRS is a validated, self reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11- point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity. Subjects were considered responders if they had at least a 4-point reduction from Baseline in weekly average WI-NRS at Week 10.

End point type	Secondary

End point timeframe:

At Week 4

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Percentage of subjects				
number (not applicable)				
Success	11.49	12.63		
Failure	88.51	87.37		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At Week 4

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.75
Method	Cochran-Mantel-Haenszel

Notes:

[2] - P-value from a CMH test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Secondary: Percent of Subjects With WI-NRS 4-point Responder Rate at Week 2

End point title	Percent of Subjects With WI-NRS 4-point Responder Rate at

	Week 2

End point description:

During the study, WI-NRS assessments were reported by the subject via eDiary once daily from screening/mid-screening visit through the follow-up visit. The Itch NRS is a validated, self reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11- point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity. Subjects were considered responders if they had at least a 4-point reduction from Baseline in weekly average WI-NRS at Week 10.

End point type	Secondary

End point timeframe:

At Week 2

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Percentage of Subjects				
number (not applicable)				
Success	6.76	5.55		
Failure	93.24	94.45		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At Week 2

Comparison groups	Serlopitant 5 mg v Placebo
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.674
Method	Cochran-Mantel-Haenszel

Notes:

[3] - P-value from a CMH test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Secondary: Change From Baseline in WI-NRS at Weeks 2, 4, 6, and 10

End point title	Change From Baseline in WI-NRS at Weeks 2, 4, 6, and 10

End point description:

During the study, WI-NRS assessments were reported by the subject via eDiary once daily from screening/mid-screening visit through the follow-up visit. The Itch NRS is a validated, self reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11- point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 6, and 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Score on a scale				
least squares mean (standard deviation)				
Change from Baseline at Week 2	-0.94 (± 1.470)	-1.25 (± 1.496)		
Change from Baseline at Week 4	-1.42 (± 1.908)	-1.60 (± 1.955)		
Change from Baseline at Week 6	-1.61 (± 2.105)	-1.93 (± 2.182)		
Change from Baseline at Week 10	-1.86 (± 2.334)	-2.24 (± 2.543)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At Week 2

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.06
Method	ANCOVA

Notes:

[4] - P-values, least squares means (LS Mean) and standard deviations (LS SD) from an analysis of covariance (ANCOVA) with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

At Week 4

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.401
Method	ANCOVA

Notes:

[5] - P-values, LS Mean and LS SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

At Week 6

Comparison groups	Placebo v Serlopitant 5 mg

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.185
Method	ANCOVA

Notes:

[6] - P-values, LS Mean and LS SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

At Week 10

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.164
Method	ANCOVA

Notes:

[7] - P-values, LS Mean and LS SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Secondary: Percent of Subjects With WI-NRS 3-point Responder at Weeks 2, 4, and 10

End point title	Percent of Subjects With WI-NRS 3-point Responder at Weeks 2, 4, and 10

End point description:

During the study, WI-NRS assessments were reported by the subject via eDiary once daily from screening/mid-screening visit through the follow-up visit. The Itch NRS is a validated, self reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11- point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity. Subjects were considered responders if they at least 3-point reduction from Baseline in weekly average WI-NRS.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, and 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Percentage of subjects				
number (not applicable)				
Percentage of responders at Week 2	8.11	11.89		
Percentage of responders at Weel 4	18.24	20.03		
Percentage of responders at Weel 10	25.65	37.58		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At Week 2

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.283
Method	Cochran-Mantel-Haenszel

Notes:

[8] - P-value from a CMH test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

At Week 4

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.701
Method	Cochran-Mantel-Haenszel

Notes:

[9] - P-value from a CMH test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

At Week 10

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.033
Method	Cochran-Mantel-Haenszel

Notes:

[10] - P-value from a CMH test stratified by Baseline WI-NRS used for randomization stratification. Value has been adjusted for multiple imputation.

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) to Week 10

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) to Week 10

End point description:

Dermatology Life Quality Index (DLQI) is a dermatology specific quality of life (QoL) instrument designed to assess the impact of the skin disease on a subject's QoL over the prior week. It is a ten item questionnaire that assesses overall QoL and six aspects that may affect QoL (symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment). The DLQI questions are rated by the subject as 0 (not at all) to 3 (very much). Scores range from 0 to 30 with higher scores indicating poor QoL.

End point type	Secondary

End point timeframe:

At Week 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Score on a scale				
least squares mean (standard deviation)	-4.4 (± 5.07)	-4.5 (± 5.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: At Week 10	
Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.797
Method	ANCOVA

Notes:

[11] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in DLQI Question 1 to Week 10

End point title	Change From Baseline in DLQI Question 1 to Week 10

End point description:

DLQI is a dermatology specific QoL instrument designed to assess the impact of the skin disease on a subject's QoL over the prior week. It is a ten item questionnaire that assesses overall QoL and six aspects that may affect QoL (symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment). The DLQI questions are rated by the subject as 0 (not at all) to 3 (very much). Scores range from 0 to 30 with higher scores indicating poor QoL.

End point type	Secondary

End point timeframe:

At Week 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Score on a scale				
least squares mean (standard deviation)	-0.6 (± 0.75)	-0.6 (± 0.76)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: At Week 10	
Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.845
Method	ANCOVA

Notes:

[12] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in Investigator's Global Assessment of Prurigo Nodularis Stage (IGA PN-S) to Weeks 2, 4, and 10

End point title	Change From Baseline in Investigator's Global Assessment of Prurigo Nodularis Stage (IGA PN-S) to Weeks 2, 4, and 10

End point description:

The IGA PN-S is an instrument used to assess the overall number and thickness of PN lesions at a given time point, as determined by the investigator. It consists of a 5-point scale ranging from 0 (clear) to 4 (severe). Higher scores indicate severe prurigo nodularis.

End point type	Secondary

End point timeframe:

At Weeks 2, 4 and 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Score on a scale				
least squares mean (standard deviation)				
Change from Baseline at Week 2	-0.2 (± 0.43)	-0.2 (± 0.43)		
Change from Baseline at Week 4	-0.4 (± 0.64)	-0.3 (± 0.64)		
Change from Baseline at Week 10	-0.5 (± 0.77)	-0.5 (± 0.78)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: At Week 2	
Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.385
Method	ANCOVA

Notes:

[13] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

At Week 4

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.786
Method	ANCOVA

Notes:

[14] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

At Week 10

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.502
Method	ANCOVA

Notes:

[15] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in Investigator's Global Assessment of Prurigo Nodularis Activity (IGA PN-A) to Weeks 2, 4, and 10

End point title	Change From Baseline in Investigator's Global Assessment of Prurigo Nodularis Activity (IGA PN-A) to Weeks 2, 4, and 10

End point description:

The IGA PN-A is an instrument used to assess the overall activity of PN lesions at a given time point, as determined by the investigator. It consists of a 5-point scale ranging from 0 (clear) to 4 (severe). Higher scores indicate severe prurigo nodularis.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, and 10

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Score on a scale				
least squares mean (standard deviation)				
Change from Baseline at Week 2	-0.2 (± 0.49)	-0.3 (± 0.49)		
Change from Baseline at Week 4	-0.5 (± 0.68)	-0.5 (± 0.68)		
Change from Baseline at Week 10	-0.7 (± 0.91)	-0.7 (± 0.92)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

At Week 2

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.197
Method	ANCOVA

Notes:

[16] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

At Week 4

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.694
Method	ANCOVA

Notes:

[17] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

At Week 10

Comparison groups	Placebo v Serlopitant 5 mg
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.916
Method	ANCOVA

Notes:

[18] - P-values, LS mean and SD from ANCOVA with treatment group and stratification factor as fixed effects, and baseline value as a covariate.

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAE) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAE) and Serious Adverse Events (SAEs)

End point description:

Adverse events (AEs) and serious adverse events (SAEs) were recorded from the first study drug

administration through the follow-up visit. Severity of all AEs were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events v4.03. During the period between informed consent and first study drug dose, only SAEs caused by a protocol-mandated intervention were collected.

End point type	Secondary

End point timeframe:

From screening until the Follow-up (F/U) visit which occurred 35 days (+ 7 days) after the Week 10 visit or the last dose of study drug for subjects who discontinued study drug early

End point values	Placebo	Serlopitant 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	147		
Units: Subjects				
Subjects with any TEAE	87	84		
Subjects with any related TEAE	24	30		
Subjects with any serious TEAE	2	5		
Subjects who died	0	0		
Subjects who discontinued study drug	4	13		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening until the Follow-up (F/U) visit which occurred 35 days (+ 7 days) after the Week 10 visit or the last dose of study drug for subjects who discontinued study drug early.

Adverse event reporting additional description:

AEs and SAEs were recorded from the first study drug administration through the follow-up visit. After informed consent was signed, but prior to initiation of study drug, only SAEs considered by the investigator to be caused by a protocol mandated intervention were collected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Randomized subjects received daily oral doses of placebo following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10-week treatment period.

Reporting group title	Serlopitant 5 mg

Reporting group description:

Randomized subjects received daily oral doses of serlopitant 5 mg following an initial 3-tablet loading dose on Day 1. Starting on Day 2, subjects took 1 tablet per day until the completion of the 10- week treatment period.

Serious adverse events	Placebo	Serlopitant 5 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 148 (1.35%)	5 / 147 (3.40%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Wound			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Musculoskeletal and connective tissue disorders			
Crystal arthropathy			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
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 5 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 148 (22.30%)	30 / 147 (20.41%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 148 (4.05%)	10 / 147 (6.80%)	
occurrences (all)	8	11	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 148 (4.05%)	12 / 147 (8.16%)	
occurrences (all)	6	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	23 / 148 (15.54%)	17 / 147 (11.56%)	
occurrences (all)	25	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2019	V 3.0: - Removed two key secondary efficacy endpoints - Increased study population to 280 subjects - Added optional interim analysis
16 December 2019	V 4.0: - Removed 'Change from Baseline in Dermatology Life Quality Index (DLQI) to Week 10'; Added 'WI-NRS 4-point responder rate at Week 2' - Removed 'WI-NRS 4-point responder rate at Week 2'; Added 'Change from Baseline in DLQI to Week 10'; Added 'Change from Baseline in DLQI Question 1 to Week 10' - Removed 'Change from Baseline in DLQI to Week 10'; Added 'WI-NRS 4-point responder rate at Week 2' - Changed the minimum number of observations needed to compute a week's average of WI-NRS from 1 observation to 4 observations; Removed the explanation for handling missing Week 10 DLQI data; Updated the number of random seeds needed to impute missing data - Removed 'Change from Baseline in DLQI to Week 10'; Added 'WI-NRS 4-point responder rate at Week 2'; Removed information regarding the ANCOVA model - Added information regarding the analysis of the secondary endpoints - Removed 'Graphs of laboratory values over time will also be produced.'

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported