Clinical trial results:
An Open-Label Long-Term Safety Study of Serlopitant for the Treatment of Pruritus

Summary

EudraCT number	2017-004211-40
Trial protocol	DE AT PL
Global end of trial date	08 April 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-107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03540160
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	24 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 April 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the long-term safety of serlopitant in adults with pruritus associated with prurigo nodularis (PN), atopic dermatitis (AD), or psoriasis.

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 IEC/IRB-approved consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 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	United States: 279
Country: Number of subjects enrolled	European Union: 279
Worldwide total number of subjects	558
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)	388
From 65 to 84 years	164
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 120 sites from 15 March 2018 to 08 April 2020. All participants who met the study entry criteria received daily oral doses of serlopitant 5 mg tablet.

Pre-assignment

Screening details:

Subjects attended a screening visit before receiving their first dose. All subjects underwent inclusion exclusion criteria assessment and all eligible subjects signed the informed consent before undergoing any study-related procedures.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Serlopitant 5 mg

Arm description:

Subjects received serlopitant 5 mg tablet once daily orally from Baseline Visit (Study Day 1) until the Week 52 Visit.

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

Dosage and administration details:

5 mg tablet once daily

Number of subjects in period 1[1]	Serlopitant 5 mg
Started	549
Completed	179
Not completed	370
Physician decision	8
Consent withdrawn by subject	68
COVID-19	2
Study Closure	10
Adverse event, non-fatal	20
Pregnancy	1
Lost to follow-up	18
Sponsor decision	182
Protocol deviation	1

Lack of efficacy	60

Notes:

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

Justification: Nine subjects were excluded from the safety population (all from US) due to no evidence of subject dosing and/or no post-Baseline assessment/treatment emergent adverse event.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	549	549	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.1		
standard deviation	± 14.62	-	
Gender categorical Units: Subjects			
Male	198	198	
Female	351	351	

End points

End points reporting groups

Reporting group title	Serlopitant 5 mg

Reporting group description:

Subjects received serlopitant 5 mg tablet once daily orally from Baseline Visit (Study Day 1) until the Week 52 Visit.

Primary: Number of Subjects With Treatment-emergent Adverse Events

End point title	Number of Subjects With Treatment-emergent Adverse

End point description:

Treatments emergent adverse events (TEAEs) 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	Primary

End point timeframe:

From baseline until the Follow-up (F/U) visit which occurred 35 days (+ 7 days) after the Week 52 visit or the last dose of study drug for subjects who discontinued study drug early.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed for this outcome measure.

End point values	Serlopitant 5 mg			
Subject group type	Reporting group			
Number of subjects analysed	549			
Units: Subjects				
Subjects with any TEAE	325			
Subjects with any related TEAE	55			
Subjects with any SAE	45			
Subjects with any related SAE	1			
Subjects who died	0			
Subjects who discontinued study drug due to TEAE	28			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline until the F/U visit which occurred 35 days (+ 7 days) after the Week 52 visit or the last dose of study drug for subjects who discontinued study drug early

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Serlopitant 5 mg

Reporting group description:

Subjects received serlopitant 5 mg tablet once daily orally.

Serious adverse events	Serlopitant 5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	45 / 549 (8.20%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal carcinoma			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			

subjects affected / exposed	2 / 549 (0.36%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hernia hiatus repair			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Adjustment disorder with anxiety			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Anticoagulation drug level below			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Clavicle fracture				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniofacial fracture				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscle rupture				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Arrhythmia				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				

subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular asystole			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurodegenerative disorder			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiculopathy			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Corneal perforation			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis haemorrhagic			

subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mechanical ileus				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic disorder				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis contact				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lichen planus				

subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurodermatitis			
subjects affected / exposed	3 / 549 (0.55%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fasciitis			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess jaw			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cellulitis				
subjects affected / exposed	2 / 549 (0.36%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	2 / 549 (0.36%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 549 (0.36%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Abnormal loss of weight				
subjects affected / exposed	1 / 549 (0.18%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				

subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 549 (0.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Serlopitant 5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 549 (6.56%)		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	36 / 549 (6.56%)		
occurrences (all)	42		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2018	V 1.1: Regarding the potential benefit and potential risk for the participating patients as well as the assessment of the ratio of this benefit and risk.
03 July 2018	V 2.0: -The study post-drug observation period was extended to 5 weeks from 4 weeks. -Removal of the PROMIS-PIQ associated efficacy endpoints and analyses. -Added two safety endpoints to measure change from baseline in Hospital Anxiety and Depression Scale (HADS) and the Epworth Sleepiness Scale (ESS) responses.
21 March 2019	V 3.0: Changed number of patients from 400 to 700

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 April 2020	This study was terminated prematurely due to a corporate decision to no longer pursue an indication of treatment for pruritus, and further to terminate the overall development program for serlopitant. For these reasons the statistical analysis plan was revised and the summary tables were limited to disposition, demographics, and AEs. All other results were provided as subject data listings.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated prematurely due to a corporate decision to no longer pursue an indication of treatment for pruritus, and further to terminate the overall development program for serlopitant.

Notes: