Clinical trial results:
A Randomized, Double Masked, Uncontrolled, Multicenter Phase I/II Study to Evaluate Safety and Tolerability of PAN-90806 Eye Drops, Suspension in Treatment-Naïve Participants with Neovascular Age-Related Macular Degeneration (AMD)

Summary

EudraCT number	2016-004601-14
Trial protocol	GB LV CZ HU
Global end of trial date	27 June 2019

Results information

Result version number	v1 (current)
This version publication date	26 February 2020
First version publication date	26 February 2020

Trial information

Trial identification

Sponsor protocol code	PAN-01-102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03479372
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 120693

Notes:

Sponsors

Sponsor organisation name	PanOptica, Inc
Sponsor organisation address	13 McGregor Avenue, Mt Arlington, United States, 07856
Public contact	Clinical Trial Information, PanOptica, Inc., +1 9087660899, clinical@panopticapharma.com
Scientific contact	Clinical Trial Information, PanOptica, Inc., +1 9087660899, clinical@panopticapharma.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	27 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2019
Global end of trial reached?	Yes
Global end of trial date	27 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the safety and tolerability of topical ocular PAN-90806 Eye Drops, Suspension

Protection of trial subjects:

This study was conducted according to the Declaration of Helsinki and the local laws and regulations relevant to the use of an investigational new drug. All participants signed the informed consent form prior to undergoing study-related procedures. All participants were informed fully of the nature and aims of the study Ample time was provided for the participants to read the informed consent document and ask any questions regarding the investigational drug and study requirements. Participants were informed that their participation was voluntary and that they could withdraw from the study at any time for any reason without incurring penalty or withholding treatment on the part of the investigator. Copies of the signed document were given to the participant and filed in the investigator's study file.

An independent data monitoring committee reviewed subject safety data during the course of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	51
EEA total number of subjects	31

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)	5
From 65 to 84 years	35
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 27 centers in 5 countries. Regulatory authority approval & IRB/IEC approvals were obtained prior to opening a center for recruitment. Participants were screened for the study between 27 April 2018 and 04 March 2019. Written informed consent was obtained prior to conducting any of the Screening procedures.

Pre-assignment

Screening details:

Treatment-naive patients with newly diagnosed, active, pathologic CNV associated with neovascular AMD were screened for inclusion into the study by assessing medical/ophthalmic history, visual acuity, ophthalmic examination, vital signs, ocular imaging, laboratory & pregnancy tests. Eligible participants were randomized to 1 of 3 doses of PAN-90806

Period 1

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

Blinding implementation details:

The investigational product was coded and labeled in a manner that protected the masking of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	2 mg/mL PAN-90806

Arm description: -

Arm type	Experimental
Investigational medicinal product name	PAN-90806 Eye Drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ocular use

Dosage and administration details:

Participants were instructed to administer the PAN-90806 eye drops once daily at approximately the same time every day (before bedtime was recommended) for 12 weeks.

Arm title	6 mg/mL PAN-90806

Arm description: -

Arm type	Experimental
Investigational medicinal product name	PAN-90806 Eye Drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ocular use

Dosage and administration details:

Participants were instructed to administer the PAN-90806 eye drops once daily at approximately the same time every day (before bedtime was recommended) for 12 weeks.

Arm title	10 mg/mL PAN-90806

Arm description: -

Arm type	Experimental

Investigational medicinal product name	PAN-90806 Eye Drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ocular use

Dosage and administration details:

Participants were instructed to administer the PAN-90806 eye drops once daily at approximately the same time every day (before bedtime was recommended) for 12 weeks.

Number of subjects in period 1	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806
Started	17	18	16
Completed	17	16	15
Not completed	0	2	1
Adverse event, non-fatal	-	2	1

Baseline characteristics

Reporting groups	
Reporting group title	2 mg/mL PAN-90806
Reporting group description: -	
Reporting group title	6 mg/mL PAN-90806
Reporting group description: -	
Reporting group title	10 mg/mL PAN-90806
Reporting group description: -	

Reporting group values	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806
Number of subjects	17	18	16
Age categorical			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: Subjects			
Adults (18-64 years)	1	1	3
From 65-84 years	14	11	10
85 years and over	2	6	3
Age continuous			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: years			
arithmetic mean	75.6	80.9	76.9
full range (min-max)	63 to 89	55 to 98	59 to 88
Gender categorical			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: Subjects			
Female	12	12	9
Male	5	6	7

Reporting group values	Total		
Number of subjects	51		
Age categorical			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: Subjects			
Adults (18-64 years)	5		
From 65-84 years	35		
85 years and over	11		
Age continuous			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: years			
arithmetic mean			

full range (min-max)	-		

Gender categorical			
Baseline characteristics were assessed on intent-to-treat population (ITT) population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.			
Units: Subjects			
Female	33		
Male	18		

End points

End points reporting groups

Reporting group title	2 mg/mL PAN-90806
Reporting group description: -	
Reporting group title	6 mg/mL PAN-90806
Reporting group description: -	
Reporting group title	10 mg/mL PAN-90806
Reporting group description: -	

Primary: Number of participants with treatment-related adverse events

End point title	Number of participants with treatment-related adverse

End point description:

The number of participants with treatment-related adverse events was assessed on the Safety population which consisted of all randomized participants who took at least 1 dose of study treatment. Participants were analyzed according to the treatment they actually received.

End point type	Primary

End point timeframe:

The reporting period for Adverse Events began with the signing of the informed consent document and continued until the last study visit.

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: This study was not powered for statistical analysis. Only descriptive statistics were performed on all endpoints

End point values	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	16	
Units: participants	3	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Center Subfield Thickness

End point title	Change from Baseline in Center Subfield Thickness

End point description:

Although the study was not designed nor powered to assess efficacy, potential biological responses to treatment were assessed as secondary endpoints by comparing the descriptive changes from baseline. Center Subfield Thickness (CST) was measured by the masked independent reading center. Change from baseline in CST was assessed on the ITT population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.

End point type	Secondary

End point timeframe:

At Week 12

End point values	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	16	
Units: microns				
arithmetic mean (full range (min-max))	-3.1 (-298 to 383)	-54.3 (-272 to 132)	-47.1 (-313 to 71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Ranibizumab Rescue Injections

End point title	Number of Ranibizumab Rescue Injections

End point description:

Although the study was not designed nor powered to assess efficacy, potential biological responses to treatment were assessed as secondary endpoints by comparing the descriptive changes from baseline. A reduced number or lack of need for rescue therapy with intravitreal ranibizumab was viewed as a key indicator of potential anti-VEGF biological activity following topical ocular PAN-90806 treatment. Need for rescue therapy was assessed on the ITT population which consisted of all randomized subjects who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.

End point type	Secondary

End point timeframe:

From Week 2 until final study visit

End point values	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	16	
Units: Number of injections				
arithmetic mean (full range (min-max))	0.8 (0 to 3)	0.8 (0 to 3)	0.8 (0 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Visual Acuity from Baseline

End point title	Change in Visual Acuity from Baseline

End point description:

Although the study was not designed nor powered to assess efficacy, potential biological responses to treatment were assessed as secondary endpoints by comparing the descriptive changes from baseline. Change in visual acuity was assessed on the ITT population which consisted of all randomized subjects

who received at least one dose of study drug, irrespective of the dose actually received. Subjects were analyzed as per the dose group assigned at randomization.

End point type	Secondary

End point timeframe:

Week 12

End point values	2 mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	16	
Units: letters				
arithmetic mean (full range (min-max))	-1.1 (-19 to 15)	0.6 (-16 to 26)	-1.6 (-18 to 13)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The evaluation period for adverse events began with the signing of the informed consent document and continued until the last study visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	2mg/mL PAN-90806
Reporting group description: -	
Reporting group title	6 mg/mL PAN-90806
Reporting group description: -	
Reporting group title	10 mg/mL PAN-90806
Reporting group description: -	

Serious adverse events	2mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	2mg/mL PAN-90806	6 mg/mL PAN-90806	10 mg/mL PAN-90806
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)	18 / 18 (100.00%)	15 / 16 (93.75%)
Investigations			
Corneal Staining			
subjects affected / exposed	1 / 17 (5.88%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	2 / 17 (11.76%)	2 / 18 (11.11%)	2 / 16 (12.50%)
occurrences (all)	2	2	2
Eye pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Foreign body sensation in eyes			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Lacrimation increased			
subjects affected / exposed	1 / 17 (5.88%)	2 / 18 (11.11%)	3 / 16 (18.75%)
occurrences (all)	1	2	3
Ocular discomfort			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Vision blurred			
subjects affected / exposed	2 / 17 (11.76%)	1 / 18 (5.56%)	3 / 16 (18.75%)
occurrences (all)	2	1	3

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