Clinical trial results:
A phase 2b randomized, double-masked, controlled trial to establish the safety and efficacy of intravitreous administration of Fovista™ (Anti-PDGFBB pegylated aptamer) administered in combination with Avastin® compared to Avastin® monotherapy in subjects with subfoveal neovascular age-related macular degeneration.

Summary

EudraCT number	2015-000518-23
Trial protocol	NL EE CZ HR
Global end of trial date	25 January 2017

Results information

Result version number	v1 (current)
This version publication date	28 November 2018
First version publication date	28 November 2018

Trial information

Trial identification

Sponsor protocol code	OPH1007

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ophthotech Corporation
Sponsor organisation address	One Penn Plaza, Suite 3520 , New York, United States, NY 10119
Public contact	Fang Li, Ophthotech Corporation, +1 212-845-8219, fang.li@ophthotech.com
Scientific contact	Fang Li, Ophthotech Corporation, +1 212-845-8219, fang.li@ophthotech.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	25 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 January 2017
Global end of trial reached?	Yes
Global end of trial date	25 January 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to evaluate the safety and efficacy of Fovista (E10030 or pegpleranib) intravitreous administration when administered in combination with Avastin compared to Avastin monotherapy in subjects with subfoveal choroidal neovascularization secondary to age-related macular degeneration (AMD).

Protection of trial subjects:

All subjects signed the informed consent before undergoing any study-related procedure. 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	26 April 2016
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	Netherlands: 7
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Estonia: 3
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	2
From 65 to 84 years	25

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 6 centers in 3 countries between 26 April 2016 and 25 January 2017. Written informed consent was obtained before any of the Screening details listed below were performed.

Pre-assignment

Screening details:

Medical&ophthalmologic history,protocol refraction&visual acuity,ophthalmologic examination,Goldmann Applanation Tonometry,vital signs,physical examination, performance status,ECG,color fundus photographs,Fluorescein Angiograms,Optical Coherence Tomography,laboratory&pregnancy tests&concomitant medication were assessed at screening prior to Day1

Period 1

Period 1 title	18 Months (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

It was the responsibility of the Principal Investigator to ensure that the physician assessing AEs, the VA examiner, all masked study personnel, and the subject remained masked to the subject's treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Fovista + Avastin

Arm description:

Subjects received the Avastin injection first, followed by Fovista injection.

Arm type	Experimental
Investigational medicinal product name	Fovista
Investigational medicinal product code	
Other name	E10030, pegpleranib
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects received the Avastin injection first (1.25 mg/eye), followed by the Fovista injection (1.5 mg/eye). Both active study drugs were administered as intravitreal injections. Subjects randomized to Fovista+Avastin received between 12 and 18 injections of Avastin 1.25 mg/eye and Fovista 1.5 mg/eye. Subjects were treated with study treatment, IVT Fovista in combination with IVT Avastin, every month for the first 6 doses (Day 1, Months 1, 2, 3, 4, and 5) and every other month thereafter (i.e., every 2 months: Months 7, 9, 11, 13, 15, and 17). During the non-treatment months, subjects could be treated according to the best corrected visual acuity (BCVA, hereafter referred to as VA) change from the prior visit.

Investigational medicinal product name	Avastin
Investigational medicinal product code	
Other name	Bevacizumab
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects received the Avastin injection first (1.25 mg/eye), followed by the Fovista injection (1.5 mg/eye). Both active study drugs were administered as intravitreal injections. Subjects randomized to Fovista+Avastin received between 12 and 18 injections of Avastin 1.25 mg/eye and Fovista 1.5 mg/eye. Subjects were treated with study treatment, IVT Fovista in combination with IVT Avastin, every month for the first 6 doses (Day 1, Months 1, 2, 3, 4, and 5) and every other month thereafter (i.e., every 2 months: Months 7, 9, 11, 13, 15, and 17). During the non-treatment months, subjects could be treated

according to the VA change from the prior visit.

Arm title	Sham + Avastin

Arm description:

Subjects received the Avastin injection first, followed by a Sham injection (pressure applied at the would-be injection site with a needle-less syringe hub).

Arm type	Experimental
Investigational medicinal product name	Avastin
Investigational medicinal product code	
Other name	Bevacizumab
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects received the Avastin injection first (1.25 mg/eye), followed by a Sham injection (pressure applied at the would-be injection site with a needle-less syringe hub). Avastin was administered as intravitreal injections. Subjects randomized to Sham+Avastin received between 12 and 18 injections of Avastin 1.25 mg/eye.
Subjects were treated with study treatment, Sham in combination with IVT Avastin, every month for the first 6 doses (Day 1, Months 1, 2, 3, 4, and 5) and every other month thereafter (i.e., every 2 months: Months 7, 9, 11, 13, 15, and 17). During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

Number of subjects in period 1	Fovista + Avastin	Sham + Avastin
Started	15	14
Completed	0	0
Not completed	15	14
Sponsor decision-study terminated early	15	14

Baseline characteristics

Reporting groups	
Reporting group title	Fovista + Avastin
Reporting group description:	
Subjects received the Avastin injection first, followed by Fovista injection.	
Reporting group title	Sham + Avastin
Reporting group description:	
Subjects received the Avastin injection first, followed by a Sham injection (pressure applied at the would-be injection site with a needle-less syringe hub).	

Reporting group values	Fovista + Avastin	Sham + Avastin	Total
Number of subjects	15	14	29
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	1	2
From 65-84 years	13	12	25
85 years and over	1	1	2
Age continuous			
Units: years			
arithmetic mean	74.8	75.3	
standard deviation	± 6.96	± 6.85	-
Gender categorical			
Units: Subjects			
Female	10	9	19
Male	5	5	10

End points

End points reporting groups

Reporting group title	Fovista + Avastin
Reporting group description:	
Subjects received the Avastin injection first, followed by Fovista injection.	
Reporting group title	Sham + Avastin
Reporting group description:	
Subjects received the Avastin injection first, followed by a Sham injection (pressure applied at the would-be injection site with a needle-less syringe hub).	

Primary: Mean change in visual acuity (ETDRS letters) from baseline at the Month 18 visit.

End point title	Mean change in visual acuity (ETDRS letters) from baseline at the Month 18 visit.[1]
End point description:	
The primary efficacy endpoint was the mean change in visual acuity (ETDRS letters) from baseline at the Month 18 visit.	
End point type	Primary
End point timeframe:	
Baseline at the Month 18 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: The study was terminated early. Due to the small number of subjects enrolled and treated in the study, summary statistics of change in visual acuity over time was not conducted.

End point values	Fovista + Avastin	Sham + Avastin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	14		
Units: Visual acuity (ETDRS letters)				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Randomization at Day 1 (14 days after Screening) until end of study.

Adverse event reporting additional description:

AEs were reported on the safety population (all subjects who received at least 1dose of study drug [Fovista,Avastin or Sham]). Subjects who have ever received an injection of Fovista were analyzed in the Fovista+Avastin group.Causally related occurrences included both events reported as: related to injection procedure and related to study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Fovista +Avastin

Reporting group description:

From Randomization at Day 1 (14 days after Screening) until end of study.

Reporting group title	Sham + Avastin

Reporting group description:

Subjects received the Avastin injection first, followed by a Sham injection (pressure applied at the would-be injection site with a needle-less syringe hub).

Serious adverse events	Fovista +Avastin	Sham + Avastin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fovista +Avastin	Sham + Avastin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	1 / 14 (7.14%)	
Congenital, familial and genetic disorders			

Corneal dystrophy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Blepharitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

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

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

Due to the early termination of the study and small number of subjects randomized and treated (N=29), none of the efficacy analyses (primary and secondary endpoints) planned in the protocol were conducted.

Notes: