Clinical trial results:
Role of multimodal imaging in the evaluation of anatomic alterations in neovascular Age-Related Macular Degeneration (AMD) subjects: 18 month Phase 2a open label study of Fovista™ (anti-PDGF therapy) administered in combination with anti-VEGF therapy

Summary

EudraCT number	2015-000519-42
Trial protocol	FR IT
Global end of trial date	06 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	OPH1008

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	06 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2017
Global end of trial reached?	Yes
Global end of trial date	06 January 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and biomarker responses of various regimens of Fovista™ when administered in combination with anti-VEGF agents, in treatment naïve and treatment experienced neovascular AMD subjects.

Protection of trial subjects:

All subjects signed the informed consent before undergoing any study-related procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2016
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	France: 15
Country: Number of subjects enrolled	Italy: 17
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	3
From 65 to 84 years	21
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 6 centers in France and 6 centers in Italy between 29 March 2016 and 06 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, color fundus photographs, Fluorescein Angiograms, Optical Coherence Tomography (OCT), Indocyanine Green and OCT angiography, 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	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment naive, simultaneous regimen

Arm description:

Treatment naive subjects randomized to simultaneous regimen received IVT Fovista + IVT anti-VEGF agent administered on the same day.

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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. 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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Avastin.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by

treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Eylea.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Lucentis.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

Arm title	Treatment naive, pre-treatment regimen

Arm description:

Treatment naive subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.

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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected 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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Avastin.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Eylea.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Lucentis.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

Arm title	Treatment experienced, simultaneous regimen

Arm description:

Treatment experienced subjects randomized to simultaneous regimen, received IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.

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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected 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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Avastin.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Eylea.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent Lucentis.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the VA change from the prior visit.

Arm title	Treatment experienced, pre-treatment regimen

Arm description:

Treatment experienced subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anit VEGF agent administered in combination on the same day.

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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected 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:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Avastin.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Eylea.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

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

Dosage and administration details:

There were 2 cohorts of subjects in this trial:treatment experienced and treatment naïve. Subjects in each cohort were randomized in a 1:1 ratio to either Simultaneous Treatment or Pre-treatment Regimen. Treatment experienced subjects continued to receive the same anti-VEGF agent that they received prior to entry into the study (i.e., Lucentis, Eylea or Avastin). Treatment naïve subjects were randomized in a 1:1:1 ratio to Lucentis, Eylea, or Avastin as the anti-VEGF agent.
Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent Lucentis.
All subjects were treated every month for the first 5 months (Baseline, Months 1,2,3,4), followed by treatment every 3 months (Months 7,10,13, and 16), for a total of 18 months. During the non-treatment months, subjects could be treated according to the best corrected VA change from the prior visit.

Number of subjects in period 1	Treatment naive, simultaneous regimen	Treatment naive, pre-treatment regimen	Treatment experienced, simultaneous regimen
Started	14	14	2
Completed	0	0	0
Not completed	14	14	2
Sponsor decision-study terminated early	14	14	2

Number of subjects in period 1	Treatment experienced, pre-treatment regimen
Started	2
Completed	0
Not completed	2
Sponsor decision-study terminated early	2

Baseline characteristics

Reporting groups	
Reporting group title	Treatment naive, simultaneous regimen
Reporting group description:	
Treatment naive subjects randomized to simultaneous regimen received IVT Fovista + IVT anti-VEGF agent administered on the same day.	
Reporting group title	Treatment naive, pre-treatment regimen
Reporting group description:	
Treatment naive subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.	
Reporting group title	Treatment experienced, simultaneous regimen
Reporting group description:	
Treatment experienced subjects randomized to simultaneous regimen, received IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.	
Reporting group title	Treatment experienced, pre-treatment regimen
Reporting group description:	
Treatment experienced subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anit VEGF agent administered in combination on the same day.	

Reporting group values	Treatment naive, simultaneous regimen	Treatment naive, pre-treatment regimen	Treatment experienced, simultaneous regimen
Number of subjects	14	14	2
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)	2	1	0
From 65-84 years	9	9	1
85 years and over	3	4	1
Age continuous Units: years			
arithmetic mean	75.6	76.8	85.5
standard deviation	± 9.55	± 8.42	± 2.12
Gender categorical Units: Subjects			
Female	7	8	1
Male	7	6	1

Reporting group values	Treatment experienced, pre-treatment regimen	Total	
Number of subjects	2	32	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	3	
From 65-84 years	2	21	
85 years and over	0	8	
Age continuous Units: years			
arithmetic mean	80.5		
standard deviation	± 2.12	-	
Gender categorical Units: Subjects			
Female	0	16	
Male	2	16	

End points

End points reporting groups

Reporting group title	Treatment naive, simultaneous regimen
Reporting group description:	
Treatment naive subjects randomized to simultaneous regimen received IVT Fovista + IVT anti-VEGF agent administered on the same day.	
Reporting group title	Treatment naive, pre-treatment regimen
Reporting group description:	
Treatment naive subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.	
Reporting group title	Treatment experienced, simultaneous regimen
Reporting group description:	
Treatment experienced subjects randomized to simultaneous regimen, received IVT Fovista 1.5 mg and IVT anti-VEGF agent administered in combination on the same day.	
Reporting group title	Treatment experienced, pre-treatment regimen
Reporting group description:	
Treatment experienced subjects randomized to pre-treatment regimen received initial administration of IVT Fovista 1.5 mg monotherapy and 48 hours later (2 days) followed by the administration of IVT Fovista 1.5 mg and IVT anit VEGF agent administered in combination on the same day.	

Primary: Change in Visual Acuity

End point title	Change in Visual Acuity[1]
End point description:	
End point type	Primary
End point timeframe:	
Severe Visual Acuity Loss (Proportion of subjects with >15 letter loss at Months 12 and 18)	

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	Treatment naive, simultaneous regimen	Treatment naive, pre-treatment regimen	Treatment experienced, simultaneous regimen	Treatment experienced, pre-treatment regimen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	2	2
Units: Proportion of subjects	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 1 dose of study drug [Fovista]).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	18.1

Reporting groups

Reporting group title	Treatment naive, simultaneous regimen

Reporting group description:

Treatment naive cohort, simultaneous regimen. Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).

Reporting group title	Treatment naive, pre-treatment regimen

Reporting group description:

Treatment naive cohort, pre-treatment regimen. Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).

Reporting group title	Treatment experienced, simultaneous regimen

Reporting group description:

Treatment naive cohort, simultaneous regimen. Subjects received the Fovista injection first (1.5 mg/eye), followed by the anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).

Reporting group title	Treatment experienced,pre-treatment regimen

Reporting group description:

Treatment naive cohort, pre-treatment regimen. Subjects received IVT Fovista (1.5 mg/eye) monotherapy and 48 hours later, IVT Fovista (1.5 mg/eye) in combination with anti-VEGF agent (i.e., Lucentis, Eylea or Avastin).

Serious adverse events	Treatment naive, simultaneous regimen	Treatment naive, pre-treatment regimen	Treatment experienced, simultaneous regimen
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment experienced,pre-treatment regimen		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment naive, simultaneous regimen	Treatment naive, pre-treatment regimen	Treatment experienced, simultaneous regimen
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 2 (0.00%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Treatment experienced,pre-treatment regimen		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2015	The rationale for the changes incorporated in OPH1008 Amendment A was with regard to the number of study visits where the "pre-treatment" regimen was administered. The original OPH1008 protocol design included the "pre-treatment" regimen administered at all study visits after the Induction Phase. Amendment A modified the treatment schedule to administer the "pre-treatment" regimen for the first 5 months of the study (Baseline, Month 1-Month 4). Beginning at Month 5, subjects were to be administered the simultaneous treatment regimen only. The "pre-treatment" regimen was now only administered during the Induction Phase of the study. In addition to the changes described above, a clarification to one of the inclusion criteria was made. There was also a change in the company responsible for Data management.
10 June 2016	Amendment B included the update of the ophthalmic inclusion criteria. The definition of active CNV was modified to remove requirement for fluid as objective of protocol was to assess biomarker responses of various regimens of Fovista™ when administered in combination with anti-VEGF agents. Using Snellen acuity before and after the prior anti-VEGF therapy maintains consistent visual acuity assessment, avoiding the potential for changes in visual acuity due to testing conditions. Amendment B included the update of both ophthalmic inclusion and exclusion criteria with respect to the requirement for number of prior intravitreal injections, criteria were modified to be consistent with European labeling of anti-VEGF agents where up to 3 loading doses are required. In addition, the exclusion criterion for HbA1c value ≥ 6.5% was removed as the safety profile in subjects with high HbA1c values was unremarkable. Only subjects with definitive diagnosis of diabetes mellitus or diabetic retinopathy were to be excluded. The section of the protocol concerning previous and concomitant therapy was modified to reflect the changes in the inclusion and exclusion criteria with respect to the requirement for number of prior intravitreal injections (modified to be consistent with European labeling of anti-VEGF agents where up to 3 loading doses are required). The amendment also included corrections in the text of the protocol and other administrative

Notes:

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.

The study was terminated early (due to the lack of efficacy from two controlled phase 3 studies [OPH1002 and OPH1003]) after the enrollment and treatment of 32 subjects, no subject completed the 18-month study.

Notes: