Clinical trial results:
A Phase 2A Open-Label Trial to Assess the Safety of Zimura™ (Anti-C5) Administered in Combination With Lucentis® 0.5 mg in Treatment Naïve Subjects with Neovascular Age Related Macular Degeneration

Summary

EudraCT number	2017-003923-31
Trial protocol	LV HU
Global end of trial date	18 October 2018

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	OPH2007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03362190
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IVERIC bio, Inc. (formerly Ophthotech Corporation)
Sponsor organisation address	Five Penn Plaza, Suite 2372, New York, United States,
Public contact	Medical Director, IVERIC bio, Inc., clinicaltrials@ivericbio.com
Scientific contact	Medical Director, IVERIC bio, Inc., clinicaltrials@ivericbio.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	18 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2018
Global end of trial reached?	Yes
Global end of trial date	18 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of intravitreal Zimura™ administered in combination with Lucentis® in treatment naïve subjects with NVAMD

Protection of trial subjects:

The study was conducted in full compliance with the principles of the Declaration of Helsinki and in line with the principles outlined in the Guideline for Good Clinical Practice (GCP), the International Council for Harmonisation (ICH) Tripartite Guideline (May 1997). Before initiation of the study, the protocol and the subject informed consent provisions were reviewed and approved by the appropriate independent ethics committees (IECs) for each of the centers involved in the study. Study initiation at each site began only after receiving written approval from the IEC. Prior to study entry, all subjects were informed fully of the nature and aims of the study. Ample time was provided for the subjects to read the subject information sheet and ask any questions regarding the investigational drug. Subjects were informed that their participation was voluntary and that they could withdraw from the study at any time for any reason without incurring any penalty or withholding of treatment on the part of the investigator. Before receiving any treatment related to this study, all subjects provided their written informed consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2017
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 States: 45
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Latvia: 6
Worldwide total number of subjects	64
EEA total number of subjects	19

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	49
85 years and over	10

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion: active subfoveal NVAMD, ≥50 years
Exclusion: severe cardiac disease, major surgical procedure <1 month of trial entry, clinically significant laboratory value, treatment with investigational agent <60 days of trial, women who are pregnant or nursing, known relevant serious allergies, prior AMD treatment (excl vitamin/mineral supplement)

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Monthly administration of Lucentis 0.5 mg followed 2 days later by Zimura 4mg

Arm type	Experimental
Investigational medicinal product name	Zimura
Investigational medicinal product code	
Other name	avacincaptad pegol
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 x 2 mg intravitreal injections in the study eye, administered once per month for 6 doses in total. Zimura injections were administered 2 days after the Lucentis injections.

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

Dosage and administration details:

0.5 mg/intravitreal injection in the study eye, administered once per month for 6 doses in total.

Arm title	Cohort 2

Arm description:

Monthly administration of Zimura 2mg + Lucentis 0.5 mg administered (given on the same day)

Arm type	Experimental
Investigational medicinal product name	Zimura
Investigational medicinal product code	
Other name	avacincaptad pegol
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 x 2 mg intravitreal injections in the study eye, administered once per month for 6 doses in total. Zimura injections were administered on the same day as the Lucentis injections.

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

Dosage and administration details:

0.5 mg/intravitreal injection in the study eye, administered once per month for 6 doses in total.

Arm title	Cohort 3

Arm description:

Zimura 2mg + Lucentis 0.5 mg

Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses of Lucentis)

Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg + Lucentis 0.5mg given on the same day (Total: 3 doses of Zimura and 3 doses of Lucentis)

Arm type	Experimental
Investigational medicinal product name	Zimura
Investigational medicinal product code	
Other name	avacincaptad pegol
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 x 2 mg intravitreal injections in the study eye, administered every 14 days for 3 months (Induction Phase) and once per month for the subsequent 3 months (Maintenance Phase). When applicable, Zimura injections were administered on the same day as the Lucentis injections.

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

Dosage and administration details:

0.5 mg/intravitreal injection in the study eye, administered once per month for 6 doses in total.

Arm title	Cohort 4

Arm description:

Zimura 2mg + Lucentis 0.5 mg

Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses Lucentis)

Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg followed 2 days later by Zimura 2mg + Lucentis 0.5mg (Total: 6 doses of Zimura & 3 doses Lucentis)

Arm type	Experimental
Investigational medicinal product name	Zimura
Investigational medicinal product code	
Other name	avacincaptad pegol
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 x 2 mg intravitreal injections in the study eye, administered every 14 days for 3 months (Induction Phase) and twice per month (2 days apart) for the subsequent 3 months (Maintenance Phase). When applicable, Zimura injections were administered on the same day as the Lucentis injections (day 0 during the Induction Phase and Day 2 during the Maintenance Phase).

Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	ranibizumab

Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.5 mg/intravitreal injection in the study eye, administered once per month for 6 doses in total (Day 0 during the Induction Phase and Day 2 during the Maintenance Phase).

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	10	10	22
Completed	10	10	22
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	Cohort 4
Started	22
Completed	20
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Monthly administration of Lucentis 0.5 mg followed 2 days later by Zimura 4mg	
Reporting group title	Cohort 2
Reporting group description:	
Monthly administration of Zimura 2mg + Lucentis 0.5 mg administered (given on the same day)	
Reporting group title	Cohort 3
Reporting group description:	
Zimura 2mg + Lucentis 0.5 mg Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses of Lucentis) Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg + Lucentis 0.5mg given on the same day (Total: 3 doses of Zimura and 3 doses of Lucentis)	
Reporting group title	Cohort 4
Reporting group description:	
Zimura 2mg + Lucentis 0.5 mg Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses Lucentis) Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg followed 2 days later by Zimura 2mg + Lucentis 0.5mg (Total: 6 doses of Zimura & 3 doses Lucentis)	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	10	10	22
Age categorical Units: Subjects			
≤ 18 years	0	0	0
18-64 years	2	0	2
≥ 65 years	8	10	20
Age continuous Units: years			
arithmetic mean	73.7	77.9	74.1
standard deviation	± 11.27	± 6.62	± 7.41
Gender categorical Units: Subjects			
Female	4	8	14
Male	6	2	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	10	10	21
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	10	10	22
More than one race	0	0	0
Unknown or Not Reported	0	0	0
ETDRS Visual Acuity - Study Eye			
Units: Number of letters read			
arithmetic mean	53.9	51.5	52.5
standard deviation	± 9.0	± 5.4	± 9.4

Reporting group values	Cohort 4	Total	
Number of subjects	22	64	
Age categorical			
Units: Subjects			
≤ 18 years	0	0	
18-64 years	1	5	
≥ 65 years	21	59	
Age continuous			
Units: years			
arithmetic mean	78.1		
standard deviation	± 7.40	-	
Gender categorical			
Units: Subjects			
Female	12	38	
Male	10	26	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	2	
Not Hispanic or Latino	21	62	
Unknown or Not Reported	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	22	64	
More than one race	0	0	
Unknown or Not Reported	0	0	
ETDRS Visual Acuity - Study Eye			
Units: Number of letters read			
arithmetic mean	53.2		
standard deviation	± 9.9	-	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Monthly administration of Lucentis 0.5 mg followed 2 days later by Zimura 4mg	
Reporting group title	Cohort 2
Reporting group description:	
Monthly administration of Zimura 2mg + Lucentis 0.5 mg administered (given on the same day)	
Reporting group title	Cohort 3
Reporting group description:	
Zimura 2mg + Lucentis 0.5 mg Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses of Lucentis) Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg + Lucentis 0.5mg given on the same day (Total: 3 doses of Zimura and 3 doses of Lucentis)	
Reporting group title	Cohort 4
Reporting group description:	
Zimura 2mg + Lucentis 0.5 mg Induction Phase (Day 1 - Month 2): Monthly administration of Zimura 2mg + Lucentis 0.5 mg given on the same day followed 14 days later with Zimura 2mg (Total: 6 doses of Zimura & 3 doses Lucentis) Maintenance Phase (Month 3-5): Monthly administration of Zimura 2mg followed 2 days later by Zimura 2mg + Lucentis 0.5mg (Total: 6 doses of Zimura & 3 doses Lucentis)	

Primary: Systemic Adverse Events

End point title	Systemic Adverse Events[1]
End point description:	
Number of subjects with systemic treatment-emergent Adverse Events (with calculated percentage)	
End point type	Primary
End point timeframe:	
6 months	

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 was a safety study and no formal hypothesis testing was performed.

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	22	22
Units: subjects				
all causalities (subjects)	6	5	5	11
all causalities (%)	60	50	23	50
related to study drugs (subjects)	0	0	0	0
related to study drugs (%)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Ophthalmic Adverse Events

End point title	Ophthalmic Adverse Events[2]

End point description:

Number of subjects with ophthalmic Adverse Events (with calculated percentage)

End point type	Primary

End point timeframe:

6 months

Notes:

[2] - 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 was a safety study and no formal hypothesis testing was performed.

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	22	22
Units: subjects				
all causalities - study eye (subjects)	8	4	11	15
all causalities - study eye (%)	80	40	50	68
all causalities - fellow eye (subjects)	1	1	0	2
all causalities - fellow eye (%)	10	10	0	9
related to inject procedure - study eye (subjects)	8	4	10	12
related to inject procedure - study eye (%)	80	40	45	55
related to inject procedure - fellow eye (subject)	0	0	0	0
related to inject procedure - fellow eye (%)	0	0	0	0
related to study drugs - study eye (subjects)	0	0	0	0
related to study drugs - study eye (%)	0	0	0	0
related to study drugs - fellow eye (subjects)	0	0	0	0
related to study drugs - fellow eye (%)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline - ECG

End point title	Change from baseline - ECG

End point description:

Number of patients with a change in ECG parameters from Baseline to Month 6

End point type	Other pre-specified

End point timeframe:

6 months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	22	22
Units: subjects				
No change (subjects)	7	5	18	12
No change (%)	70	50	82	55
Not Clinically Significant Change (subjects)	3	5	3	6
Not Clinically Significant Change (%)	30	50	14	27
Clinically Significant Change (subjects)	0	0	0	1
Clinically Significant Change (%)	0	0	0	5
Missing (subjects)	0	0	1	3
Missing (%)	0	0	5	14

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change from Baseline - Study Eye ETDRS Visual Acuity

End point title	Mean Change from Baseline - Study Eye ETDRS Visual Acuity

End point description:

Mean change from Baseline to Month 6 in the number of letters read by the study eye using the ETDRS Visual Acuity charts. Higher ETDRS letters represents better vision and a larger change in ETDRS letters represents better functioning.

End point type	Other pre-specified

End point timeframe:

6 months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	22	22
Units: number of letters read				
arithmetic mean (standard deviation)	9.0 (± 11.0)	10.2 (± 18.7)	10.7 (± 10.3)	9.9 (± 8.2)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change from Baseline - Vital Signs

End point title	Mean Change from Baseline - Vital Signs

End point description:

Mean change from Baseline to Month 6 in the following parameters: Pulse (beats/minute), blood pressure (mmHg), and respiration rate (breaths/minute)

End point type	Other pre-specified

End point timeframe:

6 months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	22	22
Units: units				
arithmetic mean (standard deviation)				
Pulse (beats/min)	-5.2 (± 5.92)	-2.0 (± 6.77)	0.7 (± 11.22)	0.1 (± 6.75)
Systolic blood pressure (mmHg)	-12.0 (± 15.04)	0.7 (± 8.92)	-1.9 (± 14.92)	-5.8 (± 18.24)
Diastolic blood pressure (mmHg)	-3.2 (± 7.93)	-7.9 (± 12.32)	-4.7 (± 11.83)	-0.4 (± 8.24)
Respiration rate (breaths/min)	0.6 (± 1.35)	-2.0 (± 3.77)	-1.0 (± 2.01)	-0.2 (± 2.31)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment until Month 6 (end of study)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Cohort 1
Reporting group description: -	
Reporting group title	Cohort 2
Reporting group description: -	
Reporting group title	Cohort 3
Reporting group description: -	
Reporting group title	Cohort 4
Reporting group description: -	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (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

Serious adverse events	Cohort 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	7 / 10 (70.00%)	10 / 22 (45.45%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Contusion			

subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Corneal abrasion			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Laceration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	6 / 10 (60.00%)	1 / 10 (10.00%)	5 / 22 (22.73%)
occurrences (all)	14	1	6
Vitreous floaters			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	3
Conjunctival hyperaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Punctate keratitis			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Eye pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Corneal oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Vitreous detachment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Cataract			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Retinal artery occlusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Subretinal fibrosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vitreous opacities			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hiatus hernia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Vitamin B complex deficiency			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 22 (59.09%)		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Corneal abrasion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Eye disorders			

Conjunctival haemorrhage				
subjects affected / exposed	6 / 22 (27.27%)			
occurrences (all)	12			
Vitreous floaters				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	3			
Conjunctival hyperaemia				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	5			
Punctate keratitis				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	2			
Eye pain				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	6			
Corneal oedema				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	3			
Ocular discomfort				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
Retinal haemorrhage				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
Vitreous detachment				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Cataract				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
Lacrimation increased				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Visual acuity reduced				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			

Visual impairment subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Neovascular age-related macular degeneration subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Retinal artery occlusion subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Subretinal fibrosis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Vitreous opacities subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Hiatus hernia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Psychiatric disorders			
Anxiety			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Herpes zoster subjects affected / exposed occurrences (all) Tooth infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Metabolism and nutrition disorders Vitamin B complex deficiency subjects affected / exposed occurrences (all) Vitamin D deficiency subjects affected / exposed occurrences (all)	 0 / 22 (0.00%) 0 0 / 22 (0.00%) 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

None reported