Clinical trial results:
A Phase III Randomised, Double-masked, Parallel Group, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics and Immunogenicity between SB11 (proposed ranibizumab biosimilar) and Lucentis® in Subjects with Neovascular Age-related Macular Degeneration

Summary

EudraCT number	2017-000422-36
Trial protocol	DE CZ HU GB
Global end of trial date	09 December 2019

Results information

Result version number	v1 (current)
This version publication date	09 December 2020
First version publication date	09 December 2020

Trial information

Trial identification

Sponsor protocol code	SB11-G31-AMD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Samsung Bioepis Co., Ltd.
Sponsor organisation address	107, Cheomdan-daero, Incheon, Korea, Republic of,
Public contact	Information Desk, Samsung Bioepis Co., Ltd. , 82 (32) 455 6114, bioepisinfo@samsung.com
Scientific contact	Information Desk, Samsung Bioepis Co., Ltd. , 82 (32) 455 6114, bioepisinfo@samsung.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	09 December 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the equivalence of efficacy of SB11 to Lucentis® in subjects with neovascular age-related macular degeneration

Protection of trial subjects:

Any AE in the study eye which compromised the subject's safety or well-being by ITV injection of IP at the Investigator's discretion. The IPs were withheld until the event resolved. Such events in the study eye included, but were not limited to:
- A decrease in BCVA of ≥ 30 letters compared with the last assessment of VA
- An IOP of ≥ 30 mmHg
- A retinal break

Any significant change in the posterior pole (e.g., sub-retinal hemorrhage, macular hole, vitreous hemorrhage or opacity, retinal detachment, etc.) detected with fundus examination were confirmed and documented with FP and/or FA. Based on these FP and/or FA, the Investigator decided IP withholding. The images taken at unscheduled visits were not sent to the central reading center.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 March 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	Poland: 96
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Czechia: 159
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Hungary: 142
Country: Number of subjects enrolled	India: 21
Country: Number of subjects enrolled	Russian Federation: 42
Country: Number of subjects enrolled	Korea, Republic of: 80
Country: Number of subjects enrolled	United States: 113
Worldwide total number of subjects	705
EEA total number of subjects	449

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)	98
From 65 to 84 years	529
85 years and over	78

Subject disposition

Recruitment

Recruitment details:

This study was conducted at a total of 75 study centers in 9 countries (Czech Republic, Germany, Hungary, India, Poland, Republic of Korea, Russia, United Kingdom, and United States [US]).

Pre-assignment

Screening details:

Participants who meet the eligibility criteria were randomly assigned to one of the two treatments of this study.

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, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SB11 (proposed ranibizumab biosimilar)

Arm description:

Subjects were administered SB11 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

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

Dosage and administration details:

Subjects were administered SB11 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Arm title	US Lucentis

Arm description:

Subjects were administered Lucentis® 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Arm type	Active comparator
Investigational medicinal product name	ranibizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were administered Lucentis 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Number of subjects in period 1	SB11 (proposed ranibizumab biosimilar)	US Lucentis
Started	351	354
Week 24	335	337
Completed	307	327
Not completed	44	27
Consent withdrawn by subject	16	9
Death	2	3
Other	3	2
Adverse event	7	6
IP non-compliance	9	1
Lost to follow-up	3	3
Protocol deviation	4	3

Baseline characteristics

Reporting groups	
Reporting group title	SB11 (proposed ranibizumab biosimilar)
Reporting group description:	
Subjects were administered SB11 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.	
Reporting group title	US Lucentis
Reporting group description:	
Subjects were administered Lucentis® 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.	

Reporting group values	SB11 (proposed ranibizumab biosimilar)	US Lucentis	Total
Number of subjects	351	354	705
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	74.4	73.8	
standard deviation	± 8.00	± 8.92	-
Gender categorical			
Units: Subjects			
Female	202	201	403
Male	149	153	302

End points

End points reporting groups

Reporting group title	SB11 (proposed ranibizumab biosimilar)

Reporting group description:

Subjects were administered SB11 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Reporting group title	US Lucentis

Reporting group description:

Subjects were administered Lucentis® 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Subject analysis set title	Per protocol set for CST
Subject analysis set type	Per protocol

Subject analysis set description:

This set consisted of all FAS subjects who had received the first IP injection at Week 0 (Day 1) and completed the procedures at Week 4 without any major protocol deviations that had an impact on the CST assessment. This PPS-CST was the primary analysis set for CST. Major protocol deviations that would lead to exclusion from this set were pre-defined prior to unmasking the treatment codes for analyses.

Primary: Change from Baseline in CST at Week 4

End point title	Change from Baseline in CST at Week 4

End point description:

The average retinal thickness in the central 1-mm area in the ETDRS grid (CST) was evaluated using OCT on the study eye at Screening and prior to intravitreal injection of IP

End point type	Primary

End point timeframe:

The primary endpoint was change from baseline in CST at Week 4 (based on assessment by central reading center)

End point values	SB11 (proposed ranibizumab biosimilar)	US Lucentis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	338		
Units: microns				
least squares mean (standard error)	-108.40 (± 4.65)	-100.05 (± 4.64)		

Statistical analyses

Statistical analysis title	Equivalence test
Comparison groups	SB11 (proposed ranibizumab biosimilar) v US Lucentis

Number of subjects included in analysis	680
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference
Point estimate	-8.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.446
upper limit	2.747
Variability estimate	Standard error of the mean
Dispersion value	5.65

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs (ocular or non-ocular) were recorded from the time the subject signed the written informed consent until Week 52 (EOS Visit) or ET Visit.
The SAEs that were considered to be related to the IP were collected regardless of the study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	SB11 (proposed ranibizumab biosimilar)

Reporting group description:

Subjects were administered SB11 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Reporting group title	US Lucentis

Reporting group description:

Subjects were administered Lucentis® 0.5 mg via intravitreal injection into the study eye every 4 weeks up to Week 48 (a total of 13 administrations of investigational product [IP]) unless they were discontinued early from the IP.

Serious adverse events	SB11 (proposed ranibizumab biosimilar)	US Lucentis	
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 350 (14.86%)	52 / 354 (14.69%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			

subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mantle cell lymphoma			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schwannoma			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			

subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 350 (0.86%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery embolism			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 350 (0.29%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 350 (0.57%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 350 (0.29%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			

subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			

subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	4 / 350 (1.14%)	3 / 354 (0.85%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 350 (0.57%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral circulatory failure			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	3 / 350 (0.86%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			

subjects affected / exposed	2 / 350 (0.57%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	2 / 350 (0.57%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Age-related macular degeneration			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iridocyclitis			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal pigment epithelial tear			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subretinal fluid			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			

subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitritis			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract subcapsular			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroidal neovascularisation			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	0 / 350 (0.00%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	0 / 350 (0.00%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			

subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 350 (0.00%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	3 / 350 (0.86%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Endophthalmitis			
subjects affected / exposed	2 / 350 (0.57%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia bacterial			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 350 (0.29%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	0 / 350 (0.00%)	2 / 354 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningitis aseptic			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 350 (0.00%)	1 / 354 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 350 (0.29%)	0 / 354 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SB11 (proposed ranibizumab biosimilar)	US Lucentis	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 350 (31.71%)	126 / 354 (35.59%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	24 / 350 (6.86%)	29 / 354 (8.19%)	
occurrences (all)	47	77	
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 350 (4.86%)	28 / 354 (7.91%)	
occurrences (all)	18	39	
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	26 / 350 (7.43%)	24 / 354 (6.78%)	
occurrences (all)	26	24	
Visual acuity reduced			
subjects affected / exposed	21 / 350 (6.00%)	23 / 354 (6.50%)	
occurrences (all)	27	31	
Conjunctival haemorrhage			
subjects affected / exposed	19 / 350 (5.43%)	19 / 354 (5.37%)	
occurrences (all)	23	21	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	39 / 350 (11.14%)	36 / 354 (10.17%)	
occurrences (all)	44	41	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2017	• According to the central reading center's practice, images used for assessment were selected at the reader's best knowledge • Charts used in the study were clarified • Central reading center confirmed concurrent macular abnormality, rather than in the opinion of the Investigator • Laser photocoagulation was not included in the category of surgery • Prohibited medication was added • Text related to subjects who underwent refractive or cataract surgery in the study eye was clarified • Target eye was specified • Retinal vascular disease that affected macula was excluded from exclusion criteria • Pregnancy test was performed only for female subjects of childbearing potential • Some exclusion criteria were added as per Korea MFDS's request • Proportion of subjects without intra- or sub-retinal fluid at Week 24 and Week 52 (based on assessment by central reading center) was moved to exploratory endpoint section • Number of subjects participating in PK evaluation was changed as per US FDA's request • Text related to primary efficacy endpoint analysis for BCVA and CST was clarified • Missing imputation method was clarified • Frequency of NEI VFQ-25 was changed as per US FDA's request • Text related to physical examination was clarified • Serious adverse event criteria were changed • Text related to central laboratory tests was clarified • Details of pregnancy test were clarified • Subject discontinuation from IP criterion was added as per India regulatory agency's request • Prohibited medication or therapy was revised • Period for providing Lucentis® for the treatment of fellow eye was clarified • Fundus photography/FA reading process was clarified • Interviewer for NEI VFQ-25 was clarified • Analysis set for CST was clarified • Adverse event reporting for AMD in the fellow eye was clarified • Events were added as AESI as per EMA summary of product characteristics and FDA prescribing information • Editorial changes and correction of errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported