Clinical trial results:
A Phase III Randomised, Double-masked, Parallel Group, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics, and Immunogenicity between SB15 (proposed aflibercept biosimilar) and Eylea® in Subjects with Neovascular Age-related Macular Degeneration

Summary

EudraCT number	2019-003883-28
Trial protocol	LV CZ HU HR
Global end of trial date	16 March 2022

Results information

Result version number	v1 (current)
This version publication date	14 May 2023
First version publication date	14 May 2023

Trial information

Trial identification

Sponsor protocol code	SB15-3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04450329
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Samsung Bioepis Co., Ltd.
Sponsor organisation address	76, Songdogyoyuk-ro, Yeonsu-gu, Incheon, Korea, Republic of, 21987
Public contact	Information Desk, Samsung Bioepis Co., Ltd., +82 032 728 0114, bioepisinfo@samsung.com
Scientific contact	Information Desk, Samsung Bioepis Co., Ltd., +82 032 728 0114, 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	16 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate the equivalence in efficacy of SB15 compared to Eylea® in subjects with neovascular age-related macular degeneration (AMD).

Protection of trial subjects:

If a subject experienced an AE or the subject's safety or well-being could be compromised by IVT injection of IP at the Investigator's discretion, IPs had to be withheld until the event was resolved or adequately repaired.
In case of the following events in the study eye (but not limited), IP had to be withheld:
• ≥ 30 mmHg in pre-injection IOP measurement
• A retinal break
• Active or suspected ocular and periocular infection
• Active severe intraocular inflammation
• Performed or planned intraocular surgery within the previous or next 28 days

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2020
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: 74
Country: Number of subjects enrolled	Croatia: 21
Country: Number of subjects enrolled	Czechia: 61
Country: Number of subjects enrolled	Estonia: 12
Country: Number of subjects enrolled	Hungary: 86
Country: Number of subjects enrolled	Latvia: 23
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 82
Country: Number of subjects enrolled	Russian Federation: 41
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	449
EEA total number of subjects	277

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)	56
From 65 to 84 years	363
85 years and over	30

Subject disposition

Recruitment

Recruitment details:

This study was conducted at a total of 56 investigational sites across 10 countries (Croatia, Czech Republic, Estonia, Hungary, Japan, Latvia, Poland, Republic of Korea, Russia, and United States [US])

Pre-assignment

Screening details:

Participants who meet the eligibility criteria were randomly assigned in a 1:1 ratio to one of the two treatments of this study.

Period 1

Period 1 title	Main 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	SB15

Arm description:

Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.

Arm type	Experimental
Investigational medicinal product name	SB15
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

SB15 administered via intravitreal (IVT) injection 2 mg (0.05 mL) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by 2 mg (0.05 mL) once every 8 weeks.

Arm title	Eylea

Arm description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.

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

Dosage and administration details:

Eylea administered via intravitreal (IVT) injection 2 mg (0.05 mL) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by 2 mg (0.05 mL) once every 8 weeks.

Number of subjects in period 1	SB15	Eylea
Started	224	225
Completed	219	219
Not completed	5	6
Adverse event, serious fatal	-	1
Consent withdrawn by subject	5	3
Adverse event, non-fatal	-	1
Protocol deviation	-	1

Period 2	
Period 2 title	Transition Period
Is this the baseline period?	No
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	SB15+SB15

Arm description:

Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive SB15 once every 8 weeks in transition period (Week 32 to Week 48).

Arm type	Experimental
Investigational medicinal product name	SB15
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

SB15 administered via intravitreal (IVT) injection 2 mg (0.05 mL) every 8 weeks up to Week 48.

Arm title	Eylea+SB15

Arm description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, transitioned to receive SB15 (Aflibercept) once every 8 weeks in transition period (Week 32 to Week 48).

Arm type	Experimental
Investigational medicinal product name	SB15
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

SB15 administered via intravitreal (IVT) injection 2 mg (0.05 mL) every 8 weeks up to Week 48.

Arm title	Eylea+Eylea

Arm description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive Eylea once every 8 weeks in transition period (Week 32 to Week 48).

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

Dosage and administration details:

Eylea administered via intravitreal (IVT) injection 2 mg (0.05 mL) every 8 weeks up to Week 48.

Number of subjects in period 2	SB15+SB15	Eylea+SB15	Eylea+Eylea
Started	219	111	108
Completed	215	109	101
Not completed	4	2	7
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	3	-	2
Other	-	-	1
Lost to follow-up	-	-	3
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	SB15
Reporting group description:	
Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.	
Reporting group title	Eylea
Reporting group description:	
Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.	

Reporting group values	SB15	Eylea	Total
Number of subjects	224	225	449
Age categorical			
Units: Subjects			
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)	33	23	56
From 65-84 years	180	183	363
85 years and over	11	19	30
Age continuous			
Units: years			
arithmetic mean	73.7	74.3	
standard deviation	± 8.05	± 8.09	-
Gender categorical			
Units: Subjects			
Female	118	132	250
Male	106	93	199

End points

End points reporting groups

Reporting group title	SB15
Reporting group description:	
Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.	
Reporting group title	Eylea
Reporting group description:	
Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.	
Reporting group title	SB15+SB15
Reporting group description:	
Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive SB15 once every 8 weeks in transition period (Week 32 to Week 48).	
Reporting group title	Eylea+SB15
Reporting group description:	
Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, transitioned to receive SB15 (Aflibercept) once every 8 weeks in transition period (Week 32 to Week 48).	
Reporting group title	Eylea+Eylea
Reporting group description:	
Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive Eylea once every 8 weeks in transition period (Week 32 to Week 48).	

Primary: Change from baseline in BCVA at Week 8

End point title	Change from baseline in BCVA at Week 8
End point description:	
End point type	Primary
End point timeframe:	
Week 8	

End point values	SB15	Eylea		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	224		
Units: letters				
least squares mean (standard error)	6.7 (± 0.56)	6.6 (± 0.57)		

Statistical analyses

Statistical analysis title	Change from Baseline in BCVA
Comparison groups	SB15 v Eylea

Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.71

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs (non-ocular or ocular AEs in study/fellow eye) were collected from the time when the subject signed the written informed consent until Week 56 (EOS visit) or ET visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	SB15

Reporting group description:

Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by 2 mg [0.05 mL] once every 8 weeks until re-randomization at Week 32.

Reporting group title	Eylea

Reporting group description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) every 4 weeks for the first 3 months (i.e., at Weeks 0, 4, and 8), followed by once every 8 weeks until re-randomization at Week 32.

Reporting group title	SB15+SB15

Reporting group description:

Subjects who were randomized at Week 0 to receive SB15 (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive SB15 once every 8 weeks in transition period (Week 32 to Week 48).

Reporting group title	Eylea+SB15

Reporting group description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, transitioned to receive SB15 (Aflibercept) once every 8 weeks in transition period (Week 32 to Week 48).

Reporting group title	Eylea+Eylea

Reporting group description:

Subjects who were randomized at Week 0 to receive Eylea (Aflibercept) in the Main Period, and after re-randomization at Week 32, continued to receive Eylea once every 8 weeks in transition period (Week 32 to Week 48).

Serious adverse events	SB15	Eylea	SB15+SB15
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 224 (5.36%)	15 / 224 (6.70%)	11 / 219 (5.02%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Benign gastric neoplasm			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Benign neoplasm of bladder			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Breast cancer			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Colon cancer metastatic			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic malignant melanoma			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Ovarian clear cell carcinoma			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Circulatory collapse			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Hypotension			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Varicose vein			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 224 (0.89%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Lung infiltration			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Pulmonary embolism			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Device placement issue			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Femur fracture			

subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Presyncope			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vascular disorder			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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

Vitreous haemorrhage			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Mechanical ileus			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Subileus			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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

Renal and urinary disorders			
Renal artery stenosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 219 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	2 / 219 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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
Cellulitis			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 219 (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

Serious adverse events	Eylea+SB15	Eylea+Eylea	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 111 (5.41%)	6 / 104 (5.77%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			

subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastric neoplasm			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma metastatic			

subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian clear cell carcinoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung infiltration			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device placement issue			

subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Presyncope			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vascular disorder			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Visual acuity reduced			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (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	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cholecystitis acute			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal artery stenosis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SB15	Eylea	SB15+SB15
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	12 / 219 (5.48%)
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	12 / 219 (5.48%)
occurrences (all)	0	0	12

Non-serious adverse events	Eylea+SB15	Eylea+Eylea	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 111 (3.60%)	1 / 104 (0.96%)	
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	4 / 111 (3.60%)	1 / 104 (0.96%)	
occurrences (all)	4	1	

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