



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, bioepisin@info@samsung.com |
| Scientific contact | Information Desk, Samsung Bioepis Co., Ltd. , 82 (32) 455 6114, bioepisin@info@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 | <ul style="list-style-type: none">• 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