Clinical trial results:
A Prospective, Randomized, Double-masked, Active Comparator-controlled, Multi-center, Two-arm, Phase 3 Study to Evaluate the Efficacy and Safety of Intravitreal KSI-301 Compared with Intravitreal Aflibercept in Participants with Neovascular (Wet) Age-related Macular Degeneration (wAMD)

Summary

EudraCT number	2021-000225-27
Trial protocol	ES HU LV SK
Global end of trial date	06 April 2023

Results information

Result version number	v1 (current)
This version publication date	12 July 2024
First version publication date	12 July 2024

Trial information

Trial identification

Sponsor protocol code	KS301P107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04964089
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kodiak Sciences Inc.
Sponsor organisation address	1200 Page Mill Road, Palo Alto, CA, United States, 94304
Public contact	KSI-CL-107 Trial Information , Kodiak Sciences Inc., ksi301clinical@kodiak.com
Scientific contact	KSI-CL-107 Trial Information , Kodiak Sciences Inc., ksi301clinical@kodiak.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	17 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 March 2023
Global end of trial reached?	Yes
Global end of trial date	06 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that KSI-301 5 mg is non-inferior to aflibercept 2 mg, with respect to the change in best corrected visual acuity (BCVA) from Day 1 to the average of Weeks 40, 44 and 48.

Protection of trial subjects:

The study followed the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All local regulatory requirements pertinent to safety of trial subjects were followed during the conduct of the trial. At the Investigator's discretion, treatment with pan-retinal photocoagulation laser.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2021
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: 39
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Latvia: 22
Country: Number of subjects enrolled	United States: 453
Worldwide total number of subjects	557
EEA total number of subjects	104

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)	37
From 65 to 84 years	421
85 years and over	99

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 94 sites in 7 countries

Pre-assignment

Screening details:

The study comprised a screening period of 21 days

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	KSI-301 (Treatment Group A)

Arm description:

Intravitreal injection of KSI-301 (5 mg) at Day 1 once every 4 weeks via intravitreal injection through Week 44.

KSI-301: Intravitreal Injection

Arm type	Experimental
Investigational medicinal product name	Tarcocimab tedromer
Investigational medicinal product code	KSI-301
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

5 mg via intravitreal injection

Arm title	Aflibercept (Treatment Group B)

Arm description:

Intravitreal injection of aflibercept (2 mg) once every 4 weeks for 3 monthly doses followed by intravitreal injection of aflibercept (2 mg) once every 8 weeks from Week 16 to Week 44. Sham injections will be administered at each monthly visit where an active treatment is not administered.

Aflibercept: Intravitreal Injection

Sham Procedure: The sham is a procedure that mimics an intravitreal injection. It involves pressing the blunt end of an empty syringe (without a needle) against the anesthetized eye. It will be administered to participants in both treatments arms at applicable visits to maintain masking.

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

Dosage and administration details:

2 mg via intravitreal injection

Number of subjects in period 1	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)
Started	276	281
Completed	254	267
Not completed	22	14
Adverse event, serious fatal	4	3
Participant moved to different state	1	-
Consent withdrawn by subject	7	6
Physician decision	1	-
Non-compliance with study schedule	1	-
Adverse event, non-fatal	3	3
Lost to follow-up	2	2
Progressive disease	3	-

Baseline characteristics

Reporting groups	
Reporting group title	KSI-301 (Treatment Group A)

Reporting group description:

Intravitreal injection of KSI-301 (5 mg) at Day 1 once every 4 weeks via intravitreal injection through Week 44.

KSI-301: Intravitreal Injection

Reporting group title	Aflibercept (Treatment Group B)

Reporting group description:

Intravitreal injection of aflibercept (2 mg) once every 4 weeks for 3 monthly doses followed by intravitreal injection of aflibercept (2 mg) once every 8 weeks from Week 16 to Week 44. Sham injections will be administered at each monthly visit where an active treatment is not administered.

Aflibercept: Intravitreal Injection

Sham Procedure: The sham is a procedure that mimics an intravitreal injection. It involves pressing the blunt end of an empty syringe (without a needle) against the anesthetized eye. It will be administered to participants in both treatments arms at applicable visits to maintain masking.

Reporting group values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)	Total
Number of subjects	276	281	557
Age categorical Units: Subjects			
Adults (18-64 years)	19	18	37
From 65-84 years	209	212	421
85 years and over	48	51	99
Age continuous Units: years			
arithmetic mean	76.9	77.2	
standard deviation	± 8.21	± 7.84	-
Gender categorical Units: Subjects			
Female	159	180	339
Male	117	101	218
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	2	1	3
Black or African American	2	0	2
Native Hawaiian or Other Pacific Islander	0	2	2
White	269	276	545
Multiple	3	0	3
Other	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	16	14	30
Not Hispanic or Latino	260	267	527
Unknown or Not Reported	0	0	0

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set defined as all randomized subjects who received at least one treatment injection. Subjects will be analyzed according to their randomized treatment

Reporting group values	Full Analysis Set		
Number of subjects	557		
Age categorical Units: Subjects			
Adults (18-64 years)	37		
From 65-84 years	421		
85 years and over	99		
Age continuous Units: years			
arithmetic mean	77		
standard deviation	± 8.02		
Gender categorical Units: Subjects			
Female	339		
Male	218		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	3		
Black or African American	2		
Native Hawaiian or Other Pacific Islander	2		
White	545		
Multiple	3		
Other	1		
Ethnicity Units: Subjects			
Hispanic or Latino	30		
Not Hispanic or Latino	527		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	KSI-301 (Treatment Group A)

Reporting group description:

Intravitreal injection of KSI-301 (5 mg) at Day 1 once every 4 weeks via intravitreal injection through Week 44.

KSI-301: Intravitreal Injection

Reporting group title	Aflibercept (Treatment Group B)

Reporting group description:

Intravitreal injection of aflibercept (2 mg) once every 4 weeks for 3 monthly doses followed by intravitreal injection of aflibercept (2 mg) once every 8 weeks from Week 16 to Week 44. Sham injections will be administered at each monthly visit where an active treatment is not administered.

Aflibercept: Intravitreal Injection

Sham Procedure: The sham is a procedure that mimics an intravitreal injection. It involves pressing the blunt end of an empty syringe (without a needle) against the anesthetized eye. It will be administered to participants in both treatments arms at applicable visits to maintain masking.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set defined as all randomized subjects who received at least one treatment injection. Subjects will be analyzed according to their randomized treatment

Primary: Mean Change in Best Corrected Visual Acuity (BCVA) From Day 1 to the Average of Non-missing BCVA Values of Weeks 40, 44 and 48

End point title	Mean Change in Best Corrected Visual Acuity (BCVA) From Day 1 to the Average of Non-missing BCVA Values of Weeks 40, 44 and 48

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity.

End point type	Primary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: ETDRS Letters				
least squares mean (standard error)	2.5 (± 0.78)	4.6 (± 0.76)		

Statistical analyses

Statistical analysis title	Change in BCVA from baseline to avg of W40,W44,W48
Comparison groups	KSI-301 (Treatment Group A) v Aflibercept (Treatment Group B)
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.0083 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.1
Confidence interval	
level	95.03 %
sides	2-sided
lower limit	-3.88
upper limit	-0.29
Variability estimate	Standard error of the mean
Dispersion value	0.91

Notes:

[1] - The maximum clinically acceptable true difference between KSI-301 and aflibercept participants to be considered non-inferior is 4.5 ETDRS letters, i.e. the non-inferiority margin (NI) is 4.5 letters.
[2] - MMRM model with treatment, visit, treatment by visit interaction, randomization stratification factors, and continuous baseline BCVA as covariates.

Secondary: Mean Change in BCVA by Visit Over Time

End point title	Mean Change in BCVA by Visit Over Time

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: ETDRS Letters				
arithmetic mean (standard deviation)				
Week 2 (n=270,275)	2.8 (± 6.48)	2.9 (± 7.12)		
Week 4 (n=273,278)	3.4 (± 7.05)	4.2 (± 7.29)		
Week 8 (n=274,274)	3.7 (± 8.52)	5.1 (± 7.86)		
Week 12 (n=267,274)	3.8 (± 8.83)	5.4 (± 7.90)		
Week 16 (n=264,274)	3.6 (± 9.09)	4.9 (± 8.54)		
Week 20 (n=262,275)	3.9 (± 9.6)	5.7 (± 8.97)		
Week 24 (n=261,270)	4.5 (± 9.29)	6.0 (± 9.45)		
Week 28 (n=257,263)	4.5 (± 9.75)	6.1 (± 9.49)		
Week 32 (n=252,268)	3.9 (± 10.32)	6.1 (± 9.86)		
Week 36 (n=250,266)	3.7 (± 10.58)	6.1 (± 9.77)		

Week 40 (n=246,265)	4.0 (± 11.05)	5.6 (± 10.75)		
Week 44 (n=240,260)	4.7 (± 9.99)	5.9 (± 10.71)		
Week 48 (n=245,262)	3.7 (± 11.12)	5.4 (± 11.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Who Gained ≥ 5, ≥10, and ≥15 Letters from Baseline Over Time

End point title	Proportion of Participants Who Gained ≥ 5, ≥10, and ≥15 Letters from Baseline Over Time

End point description:

Categorical improvements in Best Corrected Visual Acuity (BCVA) of clinically relevant BCVA measurements corresponding to 1, 2 and 3 lines of the ETDRS vision testing chart

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: Participants				
Gain ≥5 ETDRS Letters, Week 2 (n=270,275)	100	96		
Gain ≥5 ETDRS Letters, Week 4 (n=273,278)	110	129		
Gain ≥5 ETDRS Letters, Week 8 (n=274,274)	119	151		
Gain ≥5 ETDRS Letters, Week 12 (n=267,274)	124	148		
Gain ≥5 ETDRS Letters, Week 16 (n=264,274)	119	143		
Gain ≥5 ETDRS Letters, Week 20 (n=262,275)	121	161		
Gain ≥5 ETDRS Letters, Week 24 (n=261,270)	130	156		
Gain ≥5 ETDRS Letters, Week 28 (n=257,263)	122	154		
Gain ≥5 ETDRS Letters, Week 32 (n=252,268)	132	168		
Gain ≥5 ETDRS Letters, Week 36 (n=250,266)	120	158		
Gain ≥5 ETDRS Letters, Week 40 (n=246,265)	116	156		
Gain ≥5 ETDRS Letters, Week 44 (n=240,260)	126	151		
Gain ≥5 ETDRS Letters, Week 48 (n=245,262)	111	150		

Gain ≥10 ETDRS Letters, Week 2 (n=270,275)	31	37		
Gain ≥10 ETDRS Letters, Week 4 (n=273,278)	44	54		
Gain ≥10 ETDRS Letters, Week 8 (n=274,274)	52	72		
Gain ≥10 ETDRS Letters, Week 12 (n=267,274)	55	72		
Gain ≥10 ETDRS Letters, Week 16 (n=264,274)	62	68		
Gain ≥10 ETDRS Letters, Week 20 (n=262,275)	66	86		
Gain ≥10 ETDRS Letters, Week 24 (n=261,270)	70	90		
Gain ≥10 ETDRS Letters, Week 28 (n=257,263)	66	87		
Gain ≥10 ETDRS Letters, Week 32 (n=252,268)	57	95		
Gain ≥10 ETDRS Letters, Week 36 (n=250,266)	66	81		
Gain ≥10 ETDRS Letters, Week 40 (n=246,265)	67	80		
Gain ≥10 ETDRS Letters, Week 44 (n=240,260)	67	86		
Gain ≥10 ETDRS Letters, Week 48 (n=245,262)	65	85		
Gain ≥15 ETDRS Letters, Week 2 (n=270,275)	12	11		
Gain ≥15 ETDRS Letters, Week 4 (n=273,278)	18	21		
Gain ≥15 ETDRS Letters, Week 8 (n=274,274)	24	28		
Gain ≥15 ETDRS Letters, Week 12 (n=267,274)	20	29		
Gain ≥15 ETDRS Letters, Week 16 (n=264,274)	24	33		
Gain ≥15 ETDRS Letters, Week 20 (n=262,275)	28	33		
Gain ≥15 ETDRS Letters, Week 24 (n=261,270)	33	42		
Gain ≥15 ETDRS Letters, Week 28 (n=257,263)	36	46		
Gain ≥15 ETDRS Letters, Week 32 (n=252,268)	32	37		
Gain ≥15 ETDRS Letters, Week 36 (n=250,266)	32	44		
Gain ≥15 ETDRS Letters, Week 40 (n=246,265)	33	45		
Gain ≥15 ETDRS Letters, Week 44 (n=240,260)	34	48		
Gain ≥15 ETDRS Letters, Week 48 (n=245,262)	35	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Who Lost ≥5, ≥10, and ≥15 Letters from

Baseline Over Time

End point title	Proportion of Participants Who Lost ≥5, ≥10, and ≥15 Letters from Baseline Over Time

End point description:

Categorical worsening in Best Corrected Visual Acuity (BCVA) of clinically relevant BCVA measurements corresponding to 1, 2 and 3 lines of the ETDRS vision testing chart

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: Participants				
Loss ≥5 ETDRS Letters, Week 2 (n=270,275)	20	28		
Loss ≥5 ETDRS Letters, Week 4 (n=273,278)	27	19		
Loss ≥5 ETDRS Letters, Week 8 (n=274,274)	41	22		
Loss ≥5 ETDRS Letters, Week 12 (n=267,274)	35	24		
Loss ≥5 ETDRS Letters, Week 16 (n=264,274)	35	31		
Loss ≥5 ETDRS Letters, Week 20 (n=262,275)	35	27		
Loss ≥5 ETDRS Letters, Week 24 (n=261,270)	34	31		
Loss ≥5 ETDRS Letters, Week 28 (n=257,263)	38	31		
Loss ≥5 ETDRS Letters, Week 32 (n=252,268)	41	35		
Loss ≥5 ETDRS Letters, Week 36 (n=250,266)	47	32		
Loss ≥5 ETDRS Letters, Week 40 (n=246,265)	33	41		
Loss ≥5 ETDRS Letters, Week 44 (n=240,260)	33	33		
Loss ≥5 ETDRS Letters, Week 48 (n=245,262)	39	38		
Loss ≥10 ETDRS Letters, Week 2 (n=270,275)	6	10		
Loss ≥10 ETDRS Letters, Week 4 (n=273,278)	6	4		
Loss ≥10 ETDRS Letters, Week 8 (n=274,274)	10	8		
Loss ≥10 ETDRS Letters, Week 12 (n=267,274)	15	9		
Loss ≥10 ETDRS Letters, Week 16 (n=264,274)	15	15		
Loss ≥10 ETDRS Letters, Week 20 (n=262,275)	16	14		
Loss ≥10 ETDRS Letters, Week 24 (n=261,270)	17	12		

Loss ≥10 ETDRS Letters, Week 28 (n=257,263)	21	14		
Loss ≥10 ETDRS Letters, Week 32 (n=252,268)	23	16		
Loss ≥10 ETDRS Letters, Week 36 (n=250,266)	22	18		
Loss ≥10 ETDRS Letters, Week 40 (n=246,265)	21	24		
Loss ≥10 ETDRS Letters, Week 44 (n=240,260)	18	21		
Loss ≥10 ETDRS Letters, Week 48 (n=245,262)	24	25		
Loss ≥15 ETDRS Letters, Week 2 (n=270,275)	3	4		
Loss ≥15 ETDRS Letters, Week 4 (n=273,278)	4	4		
Loss ≥15 ETDRS Letters, Week 8 (n=274,274)	4	4		
Loss ≥15 ETDRS Letters, Week 12 (n=267,274)	6	3		
Loss ≥15 ETDRS Letters, Week 16 (n=264,274)	9	5		
Loss ≥15 ETDRS Letters, Week 20 (n=262,275)	7	6		
Loss ≥15 ETDRS Letters, Week 24 (n=261,270)	7	6		
Loss ≥15 ETDRS Letters, Week 28 (n=257,263)	7	5		
Loss ≥15 ETDRS Letters, Week 32 (n=252,268)	10	9		
Loss ≥15 ETDRS Letters, Week 36 (n=250,266)	14	9		
Loss ≥15 ETDRS Letters, Week 40 (n=246,265)	18	13		
Loss ≥15 ETDRS Letters, Week 44 (n=240,260)	8	11		
Loss ≥15 ETDRS Letters, Week 48 (n=245,262)	15	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants With BCVA Snellen Equivalent of 20/40 or Better Over Time (≥69 ETDRS Letters)

End point title	Proportion of Participants With BCVA Snellen Equivalent of 20/40 or Better Over Time (≥69 ETDRS Letters)

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: Participants				
Baseline (n=276,281)	122	129		
Week 2 (n=270,275)	148	152		
Week 4 (n=273,278)	156	165		
Week 8 (n=274,274)	156	165		
Week 12 (n=267,274)	148	171		
Week 16 (n=264,274)	149	172		
Week 20 (n=262,275)	151	179		
Week 24 (n=261,270)	158	183		
Week 28 (n=257,263)	151	175		
Week 32 (n=252,268)	147	174		
Week 36 (n=250,266)	147	179		
Week 40 (n=246,265)	151	174		
Week 44 (n=240,260)	149	178		
Week 48 (n=245,262)	144	175		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants With BCVA Snellen Equivalent of 20/200 or Worse Over Time (≤38 ETDRS Letters)

End point title	Proportion of Participants With BCVA Snellen Equivalent of 20/200 or Worse Over Time (≤38 ETDRS Letters)

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: Participants				
Baseline (n=276,281)	17	15		
Week 2 (n=270,275)	11	12		

Week 4 (n=273,278)	10	14		
Week 8 (n=274,274)	11	13		
Week 12 (n=267,274)	11	12		
Week 16 (n=264,274)	11	10		
Week 20 (n=262,275)	13	13		
Week 24 (n=261,270)	11	13		
Week 28 (n=257,263)	12	13		
Week 32 (n=252,268)	14	18		
Week 36 (n=250,266)	14	13		
Week 40 (n=246,265)	14	17		
Week 44 (n=240,260)	9	15		
Week 48 (n=245,262)	15	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in OCT Central Subfield Retinal Thickness (CST) From Baseline to the Average of Weeks 40, 44 and 48 and Over Time

End point title	Mean Change in OCT Central Subfield Retinal Thickness (CST) From Baseline to the Average of Weeks 40, 44 and 48 and Over Time

End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE) as assessed by a central reading center.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	281		
Units: microns				
arithmetic mean (standard deviation)				
Week 2 (n=270,274)	-72.1 (± 83.74)	-99.9 (± 93.75)		
Week 4 (n=272,277)	-74.9 (± 98.33)	-109.4 (± 100.87)		
Week 8 (n=274,274)	-89.1 (± 121.13)	-122.2 (± 109.58)		
Week 12 (n=267,274)	-97.1 (± 118.62)	-126.3 (± 111.5)		
Week 16 (n=266,274)	-107.2 (± 110.02)	-99.2 (± 110.47)		
Week 20 (n=261,275)	-111 (± 112.97)	-125.5 (± 117.39)		
Week 24 (n=262,270)	-109.9 (± 112.82)	-101.8 (± 113.21)		

Week 28 (n=257,262)	-114.6 (± 111.47)	-124.1 (± 111.51)		
Week 32 (n=251,268)	-111.9 (± 122.05)	-104.3 (± 116.09)		
Week 36 (n=250,265)	-113.6 (± 129.84)	-124.4 (± 112.12)		
Week 40 (n=246,265)	-113.6 (± 115.34)	-103.1 (± 109.25)		
Week 44 (n=240,261)	-115.8 (± 115.81)	-129.4 (± 114.70)		
Week 48 (n=245,262)	-117 (± 114)	-109.2 (± 120.75)		
Week 40-48 Average (n=253,268)	-114.6 (± 113.92)	-113.4 (± 112.07)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) reported through Week 52 or Early Termination (ET)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	KSI-301 (Treatment Group A)

Reporting group description:

Intravitreal injection of KSI-301 (5 mg) at Day 1 once every 4 weeks via intravitreal injection through Week 44.

KSI-301: Intravitreal Injection

Reporting group title	Aflibercept (Treatment Group B)

Reporting group description:

Intravitreal injection of aflibercept (2 mg) once every 4 weeks for 3 monthly doses followed by intravitreal injection of aflibercept (2 mg) once every 8 weeks from Week 16 to Week 44. Sham injections will be administered at each monthly visit where an active treatment is not administered.

Aflibercept: Intravitreal Injection

Sham Procedure: The sham is a procedure that mimics an intravitreal injection. It involves pressing the blunt end of an empty syringe (without a needle) against the anesthetized eye. It will be administered to participants in both treatments arms at applicable visits to maintain masking.

Serious adverse events	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 276 (14.13%)	39 / 281 (13.88%)	
number of deaths (all causes)	4	3	
number of deaths resulting from adverse events	4	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	2 / 276 (0.72%)	2 / 281 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (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 / 276 (0.36%)	0 / 281 (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 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			

subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 276 (0.00%)	2 / 281 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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			
Asthenia			
subjects affected / exposed	2 / 276 (0.72%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sudden death			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infusion site extravasation			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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			
Respiratory failure			
subjects affected / exposed	3 / 276 (1.09%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 276 (0.72%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Intraocular pressure increased - Study Eye			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (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			
Hip fracture			
subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 276 (0.00%)	2 / 281 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acetabulum fracture			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			

subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomal hernia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 276 (0.72%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 276 (0.36%)	3 / 281 (1.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 276 (0.36%)	2 / 281 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			

subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mitral valve incompetence			

subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paralysis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyskinesia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			

subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 276 (0.00%)	4 / 281 (1.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (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 detachment - Study Eye			
subjects affected / exposed	3 / 276 (1.09%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain - Study Eye			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis - Study Eye			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis necrotising			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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 / 276 (0.36%)	0 / 281 (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 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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	1 / 276 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 276 (0.72%)	3 / 281 (1.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	2 / 276 (0.72%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 276 (0.72%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 276 (0.72%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis - Study Eye			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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 / 276 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 281 (0.36%)	
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	KSI-301 (Treatment Group A)	Aflibercept (Treatment Group B)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 276 (39.86%)	80 / 281 (28.47%)	
Investigations			
Intraocular pressure increased - Study Eye			
subjects affected / exposed	15 / 276 (5.43%)	2 / 281 (0.71%)	
occurrences (all)	17	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 276 (6.16%)	14 / 281 (4.98%)	
occurrences (all)	17	14	
Eye disorders			
Neovascular age-related macular degeneration - Fellow Eye			
subjects affected / exposed	22 / 276 (7.97%)	15 / 281 (5.34%)	
occurrences (all)	23	16	
Vitreous floaters - Study Eye			
subjects affected / exposed	21 / 276 (7.61%)	7 / 281 (2.49%)	
occurrences (all)	23	7	
Conjunctival haemorrhage - Study Eye			
subjects affected / exposed	20 / 276 (7.25%)	11 / 281 (3.91%)	
occurrences (all)	26	17	
Infections and infestations			
COVID-19			
subjects affected / exposed	34 / 276 (12.32%)	35 / 281 (12.46%)	
occurrences (all)	35	35	
Urinary tract infection			
subjects affected / exposed	15 / 276 (5.43%)	16 / 281 (5.69%)	
occurrences (all)	23	21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2022	Version 2.0 Major changes include extension of study by 8 weeks per patient, with addition of two additional study treatment visits at weeks 40 and 44; and change in primary efficacy endpoint timing from week 40 to average of weeks 40, 44, and 48.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None specified

Notes: