Clinical trial results:
A Prospective, Randomized, Double-masked, Sham-controlled, Multi-center, Two-arm, Phase 3 Study to Evaluate the Efficacy and Safety of Intravitreal KSI-301 in Participants with Moderately Severe to Severe Non-proliferative Diabetic Retinopathy (NPDR)

Summary

EudraCT number	2020-001064-29
Trial protocol	SK ES LV CZ
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	08 September 2024
First version publication date	08 September 2024

Trial information

Trial identification

Sponsor protocol code	KS301P106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05066230
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-106 Trial Information, Kodiak Sciences Inc., ksi301clinical@kodiak.com
Scientific contact	KSI-CL-106 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	26 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 August 2023
Global end of trial reached?	Yes
Global end of trial date	31 August 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 superior to sham treatment, with respect to proportion of eyes improving ≥2 steps on Diabetic Retinopathy Severity Scale (DRSS) from baseline at Week 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	30 August 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: 1
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	United States: 243
Worldwide total number of subjects	253
EEA total number of subjects	10

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)	191
From 65 to 84 years	62
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited based on physician referral at 52 medical centers between September 2021 and August 2022. The first participant was enrolled on 07 September 2021 and the last on 25 August 2022.

Pre-assignment

Screening details:

Of 560 enrolled participants, 253 met eligibility criteria and were randomized to treatment.

Period 1

Period 1 title	Primary Study (Through Week 48)
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): three initiating doses, and then every 24 weeks through Week 92

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	Sham - Treatment Group B

Arm description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Arm type	Sham Comparator

No investigational medicinal product assigned in this arm

Number of subjects in period 1	KSI-301 - Treatment Group A	Sham - Treatment Group B
Started	128	125
Completed	120	115
Not completed	8	10
Adverse event, serious fatal	1	1
Consent withdrawn by subject	4	2

Non-compliance with study schedule	-	1
Adverse event, non-fatal	-	3
Participant relocated	1	-
Lost to follow-up	2	3

Period 2	
Period 2 title	After Week 48
Is this the baseline period?	No
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): three initiating doses, and then every 24 weeks through Week 92
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	Sham - Treatment Group B

Arm description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Arm type	Sham

No investigational medicinal product assigned in this arm

Number of subjects in period 2	KSI-301 - Treatment Group A	Sham - Treatment Group B
Started	120	115
Completed	0	0
Not completed	120	115
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	1

Non-compliance with study schedule	1	-
Lost to follow-up	3	3
Sponsor Request	115	111

Baseline characteristics

Reporting groups	
Reporting group title	KSI-301 - Treatment Group A
Reporting group description:	
Intravitreal injection of KSI-301 (5 mg): three initiating doses, and then every 24 weeks through Week 92	
Reporting group title	Sham - Treatment Group B
Reporting group description:	
Sham injection on the same schedule as Treatment Group A Sham injection: The sham injection 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 is performed to maintain masking of the study.	

Reporting group values	KSI-301 - Treatment Group A	Sham - Treatment Group B	Total
Number of subjects	128	125	253
Age categorical Units: Subjects			
Adults (18-64 years)	96	95	191
From 65-84 years	32	30	62
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.4	57.0	
standard deviation	± 11.39	± 9.63	-
Gender categorical Units: Subjects			
Female	51	56	107
Male	77	69	146
Race Units: Subjects			
American Indian or Alaska Native	0	2	2
Asian	3	3	6
Black or African American	13	23	36
Native Hawaiian or Other Pacific Islander	0	0	0
White	108	96	204
Multiple	2	0	2
Other	2	1	3
Ethnicity Units: Subjects			
Hispanic or Latino	57	52	109
Not Hispanic or Latino	71	73	144
ETDRS Diabetic Retinopathy Severity Score at Baseline Units: Subjects			
DRSS Level <=47	46	45	91
DRSS Level >=53	82	80	162

End points

End points reporting groups

Reporting group title	KSI-301 - Treatment Group A

Reporting group description:

Intravitreal injection of KSI-301 (5 mg): three initiating doses, and then every 24 weeks through Week 92

Reporting group title	Sham - Treatment Group B

Reporting group description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Reporting group title	KSI-301 - Treatment Group A

Reporting group description:

Intravitreal injection of KSI-301 (5 mg): three initiating doses, and then every 24 weeks through Week 92
KSI-301: Intravitreal injection

Reporting group title	Sham - Treatment Group B

Reporting group description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Subject analysis set title	Primary Study
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set defined as all randomized subjects who received any study treatment (KSI-301 or sham) and have gradable DRSS value at baseline. Subjects will be analyzed according to their randomized treatment.

Primary: Percentage of Patients Improving ≥2 Steps on DRSS

End point title	Percentage of Patients Improving ≥2 Steps on DRSS

End point description:

Percentage of patients improving ≥2 steps on the Diabetic Retinopathy Severity Scale (DRSS) from baseline at Week 48 using last observation carried forward (LOCF)

End point type	Primary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	52	2		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for Percentage of Patients
Comparison groups	KSI-301 - Treatment Group A v Sham - Treatment Group B
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference of weighted percentage
Point estimate	39.7
Confidence interval	
level	95.02 %
sides	2-sided
lower limit	31.3
upper limit	48.1

Notes:

[1] - Cochran-Mantel-Haentzel test stratified by baseline DRSS level (≤level 47 vs. ≥level 53) and HbA1c level (≤8.5% vs. >8.5%)

Secondary: Percentage of Patients Developing Any Sight-Threatening Complication

End point title	Percentage of Patients Developing Any Sight-Threatening Complication

End point description:

Percentage of patients developing any of the following Sight-Threatening Complication: Proliferative Diabetic Retinopathy (PDR), Anterior segment neovascularization (ASNV), Vitreous hemorrhage or tractional retinal detachment believed to be due to PDR, or Diabetic Macular Edema (DME) from baseline through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	3	26		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for Percentage of Patients
Comparison groups	KSI-301 - Treatment Group A v Sham - Treatment Group B

Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference of weighted percentage
Point estimate	-18.7
Confidence interval	
level	95.02 %
sides	2-sided
lower limit	-26.2
upper limit	-11.2

Notes:

[2] - Cochran-Mantel-Haentzel test stratified by baseline DRSS level (≤level 47 vs. ≥level 53) and HbA1c level (≤8.5% vs. >8.5%).

Secondary: Percentage of Patients Improving ≥3 Steps on DRSS

End point title	Percentage of Patients Improving ≥3 Steps on DRSS

End point description:

Percentage of patients improving ≥3 steps on the Diabetic Retinopathy Severity Scale (DRSS) from baseline at Week 48 using last observation carried forward (LOCF)

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	7	0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for Percentage of Patients
Comparison groups	KSI-301 - Treatment Group A v Sham - Treatment Group B
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0058 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference of weighted percentage
Point estimate	5.6
Confidence interval	
level	95.02 %
sides	2-sided
lower limit	1.6
upper limit	9.5

Notes:

[3] - Cochran-Mantel-Haentzel test stratified by baseline DRSS level (≤level 47 vs. ≥level 53), HbA1c level (≤8.5% vs. >8.5%).

Secondary: Percentage of Patients Developing PDR

End point title	Percentage of Patients Developing PDR
End point description:	
Percentage of patients developing Proliferative Diabetic Retinopathy (PDR) from baseline through Week 48	
End point type	Secondary
End point timeframe:	
Day 1 to Week 48	

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	2	10		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for Percentage of Patients
Comparison groups	KSI-301 - Treatment Group A v Sham - Treatment Group B
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0149 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference of weighted percentage
Point estimate	-6.5
Confidence interval	
level	95.02 %
sides	2-sided
lower limit	-11.8
upper limit	-1.3

Notes:

[4] - Cochran-Mantel-Haentzel test stratified by baseline DRSS level (≤level 47 vs. ≥level 53) and HbA1c level (≤8.5% vs. >8.5%).

Secondary: Percentage of Patients Developing PDR or ASNV

End point title	Percentage of Patients Developing PDR or ASNV
End point description:	
Percentage of patients developing Proliferative Diabetic Retinopathy (PDR) or Anterior segment neovascularization (ASNV) from baseline through Week 48	
End point type	Secondary
End point timeframe:	
Day 1 to Week 48	

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants				
Percentage of Patients Developing PDR or ASNV	2	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Developing Vitreous Hemorrhage or Tractional Retinal Detachment Believed to be Due to PDR

End point title	Percentage of Patients Developing Vitreous Hemorrhage or Tractional Retinal Detachment Believed to be Due to PDR

End point description:

Percentage of patients developing vitreous hemorrhage or tractional retinal detachment believed to be due to Proliferative Diabetic Retinopathy (PDR) from baseline through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients developing DME

End point title	Percentage of patients developing DME

End point description:

Percentage of patients developing Diabetic Macular Edema (DME) from baseline through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants	1	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With a ≥2-step or ≥3-step Worsening on DRSS

End point title	Percentage of Patients With a ≥2-step or ≥3-step Worsening on DRSS

End point description:

Percentage of patients with a ≥2-step or ≥3-step worsening on the Diabetic Retinopathy Severity Scale (DRSS) from baseline at Week 48 using last observation carried forward (LOCF). The Diabetic Retinopathy Disease Severity Scale (DRSS) may be used to describe overall retinopathy severity as well as the change in severity over time. Severity range from level 10 (DR absent) to level 85 (advanced proliferative DR: posterior fundus obscured, or center of macula detached).

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants				
number (not applicable)				
Patients with a ≥2-step worsening on DRSS (n)	1	5		
Patients with a ≥2-step worsening on DRSS (%)	0.78	4		
Patients with a ≥3-step worsening on DRSS (n)	0	3		
Patients with a ≥3-step worsening on DRSS (%)	0	2.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Who Lost ≥5, ≥10, or ≥15 Letters in BCVA

End point title	Percentage of Patients Who Lost ≥5, ≥10, or ≥15 Letters in BCVA

End point description:

Percentage of patients who lost ≥5, ≥10, or ≥15 letters in Best-corrected Visual Acuity (BCVA) from baseline by visit over time

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Participants				
number (not applicable)				
lost ≥ 5 letters from baseline-Wk 8 (N analysed)	127	123		
lost ≥ 5 letters from baseline-Wk 8 (n)	8	15		
lost ≥ 5 letters from baseline-Wk 8 (%)	6.3	12.2		
lost ≥ 5 letters from baseline-Wk 20 (N analysed)	122	109		
lost ≥ 5 letters from baseline-Wk 20 (n)	15	15		
lost ≥ 5 letters from baseline-Wk 20 (%)	12.3	13.76		
lost ≥ 5 letters from baseline-Wk 32 (N analysed)	117	99		
lost ≥ 5 letters from baseline-Wk 32 (n)	17	10		
lost ≥ 5 letters from baseline-Wk 32 (%)	14.53	10.1		
lost ≥ 5 letters from baseline-Wk 44 (N analysed)	109	90		
lost ≥ 5 letters from baseline-Wk 44 (n)	12	8		
lost ≥ 5 letters from baseline-Wk 44 (%)	11.01	8.89		
lost ≥ 5 letters from baseline-Wk 48 (N analysed)	114	91		
lost ≥ 5 letters from baseline-Wk 48 (n)	14	11		
lost ≥ 5 letters from baseline-Wk 48 (%)	12.28	12.09		
lost ≥10 letters from baseline-Wk 8 (N analysed)	127	123		
lost ≥10 letters from baseline-Wk 8 (n)	2	3		
lost ≥10 letters from baseline-Wk 8 (%)	1.57	2.44		
lost ≥10 letters from baseline-Wk 20 (N analysed)	122	109		
lost ≥10 letters from baseline-Wk 20 (n)	2	4		
lost ≥10 letters from baseline-Wk 20 (%)	1.64	3.67		
lost ≥10 letters from baseline-Wk 32 (N analysed)	117	99		
lost ≥10 letters from baseline-Wk 32 (n)	5	1		

lost ≥10 letters from baseline-Wk 32 (%)	4.27	1.01		
lost ≥10 letters from baseline-Wk 44 (N analysed)	109	90		
lost ≥10 letters from baseline-Wk 44 (n)	4	2		
lost ≥10 letters from baseline-Wk 44 (%)	3.67	2.22		
lost ≥10 letters from baseline-Wk 48 (N analysed)	114	91		
lost ≥10 letters from baseline-Wk 48 (n)	5	1		
lost ≥10 letters from baseline-Wk 48 (%)	4.39	1.1		
lost ≥15 letters from baseline-Wk 8 (N analysed)	127	123		
lost ≥15 letters from baseline-Wk 8 (n)	1	1		
lost ≥15 letters from baseline-Wk 8 (%)	0.79	0.81		
lost ≥15 letters from baseline-Wk 20 (N analysed)	122	109		
lost ≥15 letters from baseline-Wk 20 (n)	1	1		
lost ≥15 letters from baseline-Wk 20 (%)	0.82	0.92		
lost ≥15 letters from baseline-Wk 32 (N analysed)	117	99		
lost ≥15 letters from baseline-Wk 32 (n)	4	0		
lost ≥15 letters from baseline-Wk 32 (%)	3.42	0		
lost ≥15 letters from baseline-Wk 44 (N analysed)	109	90		
lost ≥15 letters from baseline-Wk 44 (n)	0	0		
lost ≥15 letters from baseline-Wk 44 (%)	0	0		
lost ≥15 letters from baseline-Wk 48 (N analysed)	114	91		
lost ≥15 letters from baseline-Wk 48 (n)	3	0		
lost ≥15 letters from baseline-Wk 48 (%)	2.63	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Levelopment of PDR, ASNV, or DME

End point title	Time to First Levelopment of PDR, ASNV, or DME

End point description:

Time to first development of Proliferative Diabetic Retinopathy (PDR), Anterior segment neovascularisation (ASNV), or Diabetic Macular Edema (DME) through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128[5]	125[6]		
Units: Months				
median (confidence interval 95%)				
Time to 1st development of PDR, ASNV or DME	0 (0 to 0)	0 (0 to 0)		

Notes:

[5] - 0 = Not available due to small number of PDR, ASNV and DME events

[6] - 0 = Not available due to small number of PDR, ASNV and DME events

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Development of PDR or ASNV

End point title	Time to First Development of PDR or ASNV

End point description:

Time to first development of Proliferative Diabetic Retinopathy (PDR) or Anterior Segment Neovascularization (ASNV) through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128[7]	125[8]		
Units: Months				
median (confidence interval 95%)				
Time to first development of PDR or ASNV	0 (0 to 0)	0 (0 to 0)		

Notes:

[7] - 0 = Not available due to small number of PDR and ASNV events

[8] - 0 = Not available due to small number of PDR and ASNV events

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Development of Vitreous Hemorrhage or Tractional Retinal Detachment Believed to be Due to PDR

End point title	Time to First Development of Vitreous Hemorrhage or Tractional Retinal Detachment Believed to be Due to PDR

End point description:

Time to first development of vitreous hemorrhage (VH) or tractional retinal detachment (TRD) believed to be due to Proliferative Diabetic Retinopathy (PDR) through Week 48

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128[9]	125[10]		
Units: Months				
median (confidence interval 95%)				
Time to 1st development of VH or TRD	0 (0 to 0)	0 (0 to 0)		

Notes:

[9] - 0 = Not available due to small number of vitreous haemorrhage & tractional retinal detachment

[10] - 0 = Not available due to small number of vitreous haemorrhage & tractional retinal detachment

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change in OCT CST

End point title	Mean Change in OCT CST

End point description:

Mean change in Optical Coherence Tomography (OCT) central subfield retinal thickness (CST) from baseline by visit over time

End point type	Other pre-specified

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: Microns				
arithmetic mean (standard deviation)				
Week 8 (n = 127, 123)	-9.8 (± 10.64)	4.5 (± 17.22)		
Week 20 (n = 122, 109)	-12.8 (± 13.42)	6.6 (± 28.99)		
Week 32 (n = 117, 99)	-13.9 (± 14.88)	5.2 (± 27.86)		
Week 44 (n = 109, 90)	-8.9 (± 19.71)	-0.5 (± 17.12)		
Week 48 (n = 114, 91)	-15.2 (± 16.35)	-0.7 (± 15.76)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Change in BCVA

End point title	Mean Change in BCVA

End point description:

Mean change in Best-corrected Visual Acuity (BCVA) from baseline by visit over time

End point type	Other pre-specified

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	125		
Units: ETDRS Letters				
arithmetic mean (standard deviation)				
Week 8 (n = 127, 123)	1.3 (± 5.02)	0.2 (± 4.80)		
Week 20 (n = 122, 109)	1.1 (± 5.22)	0.3 (± 6.29)		
Week 32 (n = 117, 99)	0.9 (± 8.68)	1.2 (± 4.87)		
Week 44 (n = 109, 90)	1.0 (± 5.63)	1.6 (± 5.55)		
Week 48 (n = 114, 91)	1.1 (± 6.44)	1.5 (± 5.49)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to First Development of DME

End point title	Time to First Development of DME

End point description:

Time to first development of Diabetic Macular Edema (DME) through Week 48

End point type	Other pre-specified

End point timeframe:

Day 1 to Week 48

End point values	KSI-301 - Treatment Group A	Sham - Treatment Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128[11]	125[12]		
Units: Months				
median (confidence interval 95%)				
Time to first development of DME	0 (0 to 0)	0 (0 to 0)		

Notes:
[11] - 0 = Not available due to small number of DME events
[12] - 0 = Not available due to small number of DME events

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) reported through the End of Study 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 (Day 1 to Week 48)

Reporting group description:

Intravitreal injection of KSI-301 (5 mg): three initiating doses, and then every 24 weeks through Week 92
KSI-301: Intravitreal injection

Reporting group title	Treatment Group B (Day 1 to Week 48)

Reporting group description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Reporting group title	KSI-301 - Treatment Group A (Post Week 48 to End of Study)

Reporting group description:

Intravitreal injection of KSI-301 (5 mg): three initiating doses, and then every 24 weeks through Week 92
KSI-301: Intravitreal injection

Reporting group title	Treatment Group B (Post Week 48 to End of Study)

Reporting group description:

Sham injection on the same schedule as Treatment Group A
Sham injection: The sham injection 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 is performed to maintain masking of the study.

Serious adverse events	KSI-301 - Treatment Group A (Day 1 to Week 48)	Treatment Group B (Day 1 to Week 48)	KSI-301 - Treatment Group A (Post Week 48 to End of Study)
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 128 (14.06%)	12 / 125 (9.60%)	8 / 120 (6.67%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Hypertensive emergency			

subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	2 / 120 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Acute pulmonary oedema			
subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Periprosthetic fracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Fibula fracture			

subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	1 / 120 (0.83%)
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 disorders			
Coronary artery disease			
subjects affected / exposed	2 / 128 (1.56%)	0 / 125 (0.00%)	0 / 120 (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
Angina unstable			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Atrioventricular block			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Atrioventricular block second degree			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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 arrest			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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 congestive			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Pulseless electrical activity			

subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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 chronic			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral arteriosclerosis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Eye disorders			
Retinal vein occlusion - Fellow Eye			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Hepatobiliary disorders			
Gallbladder rupture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Portal vein thrombosis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	0 / 120 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	0 / 120 (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
Infections and infestations			
Localised infection			
subjects affected / exposed	2 / 128 (1.56%)	0 / 125 (0.00%)	0 / 120 (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
Osteomyelitis			
subjects affected / exposed	1 / 128 (0.78%)	2 / 125 (1.60%)	2 / 120 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Complicated appendicitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Infected cyst			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Sepsis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Septic shock			

subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Urinary tract infection			
subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	0 / 120 (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
Appendicitis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Cellulitis staphylococcal			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Mycoplasma infection			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Pneumonia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 125 (0.80%)	0 / 120 (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
Osteomyelitis acute			
subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 128 (0.00%)	0 / 125 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	1 / 128 (0.78%)	0 / 125 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Group B (Post Week 48 to End of Study)		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 115 (2.61%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive emergency			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired healing			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute pulmonary oedema			

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periprosthetic fracture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Atrioventricular block second degree				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulseless electrical activity				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Ischaemic stroke				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral arteriosclerosis				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 115 (0.87%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				

Deafness			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal vein occlusion - Fellow Eye			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Gallbladder rupture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Portal vein thrombosis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin ulcer			

subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Localised infection			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Complicated appendicitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infected cyst				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mycoplasma infection				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 115 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis acute				

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	KSI-301 - Treatment Group A (Day 1 to Week 48)	Treatment Group B (Day 1 to Week 48)	KSI-301 - Treatment Group A (Post Week 48 to End of Study)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 128 (38.28%)	51 / 125 (40.80%)	15 / 120 (12.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 128 (9.38%)	10 / 125 (8.00%)	2 / 120 (1.67%)
occurrences (all)	13	10	2
Eye disorders			
Cataract - Study Eye			
subjects affected / exposed	13 / 128 (10.16%)	5 / 125 (4.00%)	3 / 120 (2.50%)
occurrences (all)	14	5	3
Conjunctival haemorrhage - Study Eye			
subjects affected / exposed	9 / 128 (7.03%)	4 / 125 (3.20%)	1 / 120 (0.83%)
occurrences (all)	9	5	1
Cataract - Fellow Eye			
subjects affected / exposed	7 / 128 (5.47%)	3 / 125 (2.40%)	1 / 120 (0.83%)
occurrences (all)	7	3	1
Diabetic retinal oedema - Study Eye			

subjects affected / exposed	2 / 128 (1.56%)	18 / 125 (14.40%)	3 / 120 (2.50%)
occurrences (all)	2	19	3
Diabetic retinopathy - Study Eye			
subjects affected / exposed	2 / 128 (1.56%)	8 / 125 (6.40%)	1 / 120 (0.83%)
occurrences (all)	2	8	1
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 128 (7.03%)	6 / 125 (4.80%)	1 / 120 (0.83%)
occurrences (all)	9	7	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	15 / 128 (11.72%)	8 / 125 (6.40%)	3 / 120 (2.50%)
occurrences (all)	15	8	3

Non-serious adverse events	Treatment Group B (Post Week 48 to End of Study)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 115 (7.83%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences (all)	1		
Eye disorders			
Cataract - Study Eye			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences (all)	0		
Conjunctival haemorrhage - Study Eye			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences (all)	0		
Cataract - Fellow Eye			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences (all)	0		
Diabetic retinal oedema - Study Eye			
subjects affected / exposed	3 / 115 (2.61%)		
occurrences (all)	3		
Diabetic retinopathy - Study Eye			

subjects affected / exposed occurrences (all)	3 / 115 (2.61%) 3		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	 0 / 115 (0.00%) 0		
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all)	 2 / 115 (1.74%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2021	Version 1.1 - Changes from Version 1.0 (original protocol) include: minor editorial and administrative revisions.

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.

This study was terminated after all participants completed Wk 48 safety follow-up due to demonstration of efficacy at the Week 48 Primary Analysis. Results were not reported for some endpoints due to insufficient sample size.

Notes: