Clinical trial results:
Efficacy and Safety of Bilateral Intravitreal Injection of GS010: A Randomized, Double-Masked, Placebo-Controlled Trial in Subjects Affected with G11778A ND4 Leber Hereditary Optic Neuropathy for Up to One Year

Summary

EudraCT number	2017-002187-40
Trial protocol	BE FR GB ES NL IT
Global end of trial date	23 July 2024

Results information

Result version number	v1 (current)
This version publication date	05 March 2026
First version publication date	05 March 2026

Trial information

Trial identification

Sponsor protocol code	GS-LHON-CLIN-05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03293524
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GenSight Biologics
Sponsor organisation address	74 Rue de Faubourg Saint Antoine, Paris, France, 75012
Public contact	VP Regulatory Affairs , GenSight Biologics, 33 176217233, schekroun@gensight-biologics.com
Scientific contact	Chief Medical Officer, GenSight Biologics, 33 176217233, mtaiel@gensight-biologics.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	06 November 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 July 2024
Global end of trial reached?	Yes
Global end of trial date	23 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of intravitreal GS010 compared to placebo intravitreal injection in second affected/not yet affected eyes, at 1.5-Year post-treatment, utilizing the change from baseline of the best-corrected visual acuity (BCVA) reported with the Log of the Minimal Angle of Resolution (LogMAR), in ND4 LHON subjects with vision loss up to one year.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles established in the Declaration of Helsinki (7th revision, 2013) with the principles of Good Clinical Practice (GCP) according to the International Council for Harmonization (ICH) guideline (ICH E6 [R2]), as well as with applicable regulatory requirements.

Background therapy:

There were restrictions on the use of concomitant medications during the trial. The following medications were not permitted: IVT drug delivery to any eye within 30 days prior to the Screening Visit, and use of idebenone that was not completely discontinued at least 7 days prior to Visit 2 (Inclusion Visit).

Evidence for comparator:

No gene therapy product had been approved for the treatment of LHON at the time of the study conduct. This study included a treatment arm (Treatment Arm 2) in which each subject received IVT lenadogene nolparvovec in their first-affected eye and a placebo IVT injection in their second-affected/not-yet-affected eye

Actual start date of recruitment	12 March 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	United States: 56
Country: Number of subjects enrolled	France: 4
Worldwide total number of subjects	98
EEA total number of subjects	19

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)	10
Adults (18-64 years)	86
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

108 patients (>=15 years old) were screened for eligibility in 13 sites (Belgium, France, Italy, Spain, Taiwan, United Kingdom: 1 site each, and the United States: 7 sites). Of these, 98 were randomized: 48 to treatment arm 1 (GS010-GS010) and 50 to treatment arm 2 (GS010-placebo). The remaining 10 subjects were screen failures.

Pre-assignment

Screening details:

108 patients with the G11778A mitochondrial point mutation in the ND4 gene and vision loss of up to 1 year in one or both eyes were screened. Screening failures (10) including patients who did not meet inclusion criteria or met exclusion criteria

Period 1

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

Blinding implementation details:

Study treatments were masked and the allocation to treatment groups was not known to the investigator or other persons involved in the conduct of the study, except the site pharmacies personnel to allow for preparation of investigational products before administration, in cases of emergencies and the data safety monitoring board (DSMB). To ensure that the double-masking design of the study was maintained, GS010 and placebo were identical in appearance and storage conditions.

Arms

Are arms mutually exclusive?	Yes
Arm title	GS010-GS010

Arm description:

Patients received single IVT injection of GS010 in both their first-affected eye and their second-affected/not-yet-affected eye

Arm type	Experimental
Investigational medicinal product name	GS010/GS010
Investigational medicinal product code	GS010/GS010
Other name	Lenadogene nolparvovec
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

Patients received IVT lenadogene nolparvovec in both eyes at a droplet digital polymerase chain reaction (ddPCR) dose of 1.2/1.3E11 vg in 90 microL for each eye. Treatment could be performed either on a single day (1 IVT injection in each eye on Day 0) or on 2 consecutive days (1st IVT injection on Day -1 and 2nd IVT injection on Day 0)

Arm title	GS010-Placebo

Arm description:

Patients received single IVT injection of GS010 in their first-affected eye and placebo IVT injection in their second-affected/not-yet-affected eye

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

Patients received IVT lenadogene nolparvovec in their first-affected eye (ddPCR dose of 1.2/1.3E11 vg in a volume of 90 microL) and placebo IVT injection (volume of 90 microL) in their second-affected/not-yet-affected eye

Number of subjects in period 1	GS010-GS010	GS010-Placebo
Started	48	50
Completed	40	36
Not completed	8	14
Email by patient 9 months after final visit	-	1
Death	-	2
Non-compliant to visits	-	1
Lost to follow-up	4	4
Withdrawal by subject	4	6

Baseline characteristics

Reporting groups	
Reporting group title	GS010-GS010
Reporting group description:	
Patients received single IVT injection of GS010 in both their first-affected eye and their second-affected/not-yet-affected eye	
Reporting group title	GS010-Placebo
Reporting group description:	
Patients received single IVT injection of GS010 in their first-affected eye and placebo IVT injection in their second-affected/not-yet-affected eye	

Reporting group values	GS010-GS010	GS010-Placebo	Total
Number of subjects	48	50	98
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	3	7	10
Adults (18-64 years)	44	42	86
From 65-84 years	1	1	2
Age continuous			
Units: years			
arithmetic mean	32.4	31.8	
standard deviation	± 14.4	± 13.4	-
Gender categorical			
Units: Subjects			
Female	11	9	20
Male	37	41	78
Affected eye status			
Units: Subjects			
Unilateral	1	0	1
Bilateral	47	50	97
Current alcohol use			
Units: Subjects			
<=1 drink/day or occasionally	24	27	51
>1 to 2 drinks/day	5	5	10
>2 drinks/day	2	4	6
No use	16	13	29
Missing	1	1	2
Age at onset of the disease			
Units: years			
arithmetic mean	31.7	31.2	
standard deviation	± 14.4	± 13.4	-
Time interval of vision loss between 1st and 2nd-affected eye			
Units: days			
arithmetic mean	56.9	61.9	
standard deviation	± 66.3	± 54.1	-
Durations of disease			
Units: months			
arithmetic mean	8.3	8.3	

standard deviation	± 3.4	± 3.1	-

End points

End points reporting groups

Reporting group title	GS010-GS010
Reporting group description:	
Patients received single IVT injection of GS010 in both their first-affected eye and their second-affected/not-yet-affected eye	
Reporting group title	GS010-Placebo
Reporting group description:	
Patients received single IVT injection of GS010 in their first-affected eye and placebo IVT injection in their second-affected/not-yet-affected eye	
Subject analysis set title	Intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The intent-to-treat analysis (ITT) population consisted of all randomized subjects. The analyses were based on the planned treatment (as randomized).	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population was defined as those patients who received study drug (GS010 or Placebo) in at least one eye. Patients were classified according to treatment actually received.	

Primary: Change from baseline of the Best Corrected Visual Acuity (BCVA) reported with LogMAR at 1.5 years post-treatment

End point title	Change from baseline of the Best Corrected Visual Acuity (BCVA) reported with LogMAR at 1.5 years post-treatment
End point description:	
The primary efficacy endpoint was the change from baseline of BCVA reported with LogMAR at 1.5 year post-treatment, in the second-affected/not-yet-affected eyes of ND4 LHON patients with vision loss up to one year. LogMAR BCVA was used to represent BCVA.	
End point type	Primary
End point timeframe:	
Change from baseline of the Best Corrected Visual Acuity (BCVA) reported with LogMAR at 1.5 years post-treatment, in the second-affected/not-yet affected eyes	

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: log units				
least squares mean (standard error)	-0.09 (± 0.072)	-0.04 (± 0.071)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-GS010 v GS010-Placebo

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.101

Secondary: Change from baseline of the BCVA reported with LogMAR at 5 years post-treatment

End point title	Change from baseline of the BCVA reported with LogMAR at 5 years post-treatment

End point description:

Change from baseline of BCVA reported with LogMAR at 5 years post-treatment, in the second-affected/not-yet-affected eyes of ND4 LHON patients with vision loss up to one year. LogMAR BCVA was used to represent BCVA.

End point type	Secondary

End point timeframe:

Change from baseline of the Best Corrected Visual Acuity (BCVA) reported with LogMAR at 5 years post-treatment, in the second-affected/not-yet affected eyes

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: LogMAR				
arithmetic mean (standard deviation)	-0.13 (± 0.080)	-0.05 (± 0.079)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-GS010 v GS010-Placebo

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5086
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.112

Secondary: Proportion of patients who switched from off-chart eyes to on-chart eyes at 5 years post-treatment

End point title	Proportion of patients who switched from off-chart eyes to on-chart eyes at 5 years post-treatment

End point description:

Proportion of patients with both eyes off-chart, defined as those patients unable to read letter on the ETDRS chart, who had at least one eye on-chart, defined as those patients able to read letters on the ETDRS chart (at either 4 meters or 1 meter) at 5 years

End point type	Secondary

End point timeframe:

From baseline to 5 years post-treatment

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: Proportion of patients				
number (not applicable)	61.54	33.33		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder analyses - Improvements from nadir (gainer eyes) at 5 years

End point title	Responder analyses - Improvements from nadir (gainer eyes) at 5 years

End point description:

Proportion of patients with an improvement of at least -0.3 LogMAR (>= +15 ETDRS letters) from nadir to year 5 in at least one eye. Nadir was defined for each eye of each subject as the worst value observed from baseline to year 5

End point type	Secondary

End point timeframe:

From nadir to 5 years post-treatment

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: Percentage of patients				
number (not applicable)	68.8	66.0		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-GS010 v GS010-Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7605
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.7

Secondary: Responder analyses - Clinically Relevant Recovery from nadir at 5 years

End point title	Responder analyses - Clinically Relevant Recovery from nadir at 5 years

End point description:

Proportion of patients with clinically relevant recovery (CRR) from nadir that was defined as patient with a CRR in at least one eye - Patient with at least one eye which was on chart at nadir, and which had an improvement of at least -0.2 LogMAR from nadir, or which was off-chart at nadir but became on-chart

End point type	Secondary

End point timeframe:

From nadir to 5 years post-treatment

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: Percentage of patients				
number (not applicable)	75.0	60.0		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-Placebo v GS010-GS010
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1352
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	4.6

Secondary: Responder analyses- Clinically Relevant Benefit at 5 years	
End point title	Responder analyses- Clinically Relevant Benefit at 5 years
End point description:	
Proportion of patients who had clinically relevant stabilization (CRS), defined as eyes with LogMAR BCVA <1 at baseline and at 5 years post-treatment or had a clinically relevant recovery (CRR) from nadir	
End point type	Secondary
End point timeframe:	
From baseline to 5 years post-treatment	

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: Proportion of patients				
number (not applicable)	75.0	62.0		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-GS010 v GS010-Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1995
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	4.3

Secondary: Quality of life questionnaire: VFQ-25 - Composite score	
End point title	Quality of life questionnaire: VFQ-25 - Composite score
End point description:	
End point type	Secondary
End point timeframe:	
Change from baseline to 5 years follow up in the Visual Function Questionnaire (VFQ-25) composite score	

End point values	GS010-GS010	GS010-Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	36		
Units: points				
least squares mean (standard error)	11.8 (± 2.48)	15.0 (± 2.51)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	GS010-GS010 v GS010-Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3605
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of the ICF was signed throughout the completion of the study follow-up (Year 5)

Adverse event reporting additional description:

Patients were expected to volunteer information about adverse events that they experienced. In addition, the investigator or designee questioned the patient at each visit about adverse events and recorded these as well as other adverse events at the visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	GS010-GS010

Reporting group description:

Patients received single IVT injection of GS010 in both their first-affected eye and their second-affected/not-yet-affected eye. This population took into account the study treatment actually received by the patients

Reporting group title	GS010-Placebo

Reporting group description:

Patients received single IVT injection of GS010 in their first-affected eye and placebo IVT injection in their second-affected/not-yet affected-eye. Patients in this group took into account the study treatment actually received by the patients

Serious adverse events	GS010-GS010	GS010-Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 49 (10.20%)	6 / 49 (12.24%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	1 / 49 (2.04%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Death			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sudden cardiac death			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (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			
Muscle spasms			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			

subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
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	GS010-GS010	GS010-Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 49 (100.00%)	49 / 49 (100.00%)	
Investigations			
Gamma glutamyltransferase increased			
subjects affected / exposed	1 / 49 (2.04%)	5 / 49 (10.20%)	
occurrences (all)	1	5	
Blood glucose increased			
subjects affected / exposed	1 / 49 (2.04%)	4 / 49 (8.16%)	
occurrences (all)	1	5	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 49 (22.45%)	8 / 49 (16.33%)	
occurrences (all)	13	8	
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 49 (6.12%)	5 / 49 (10.20%)	
occurrences (all)	8	9	
Conjunctival hyperaemia			
subjects affected / exposed	6 / 49 (12.24%)	2 / 49 (4.08%)	
occurrences (all)	10	2	
Vitreous floaters			
subjects affected / exposed	6 / 49 (12.24%)	6 / 49 (12.24%)	
occurrences (all)	9	10	
Iritis			

subjects affected / exposed	7 / 49 (14.29%)	11 / 49 (22.45%)	
occurrences (all)	13	14	
Intraocular pressure increased			
subjects affected / exposed	9 / 49 (18.37%)	7 / 49 (14.29%)	
occurrences (all)	16	12	
Eye pain			
subjects affected / exposed	10 / 49 (20.41%)	8 / 49 (16.33%)	
occurrences (all)	15	9	
Uveitis			
subjects affected / exposed	11 / 49 (22.45%)	6 / 49 (12.24%)	
occurrences (all)	20	7	
Vitritis			
subjects affected / exposed	19 / 49 (38.78%)	23 / 49 (46.94%)	
occurrences (all)	40	26	
Keratic precipitates			
subjects affected / exposed	15 / 49 (30.61%)	14 / 49 (28.57%)	
occurrences (all)	31	18	
Iridocyclitis			
subjects affected / exposed	14 / 49 (28.57%)	12 / 49 (24.49%)	
occurrences (all)	33	18	
Punctate keratitis			
subjects affected / exposed	12 / 49 (24.49%)	7 / 49 (14.29%)	
occurrences (all)	25	11	
Photophobia			
subjects affected / exposed	3 / 49 (6.12%)	2 / 49 (4.08%)	
occurrences (all)	5	3	
Anterior chamber inflammation			
subjects affected / exposed	1 / 49 (2.04%)	3 / 49 (6.12%)	
occurrences (all)	2	3	
Conjunctival haemorrhage			
subjects affected / exposed	3 / 49 (6.12%)	6 / 49 (12.24%)	
occurrences (all)	5	10	
Ocular hypertension			
subjects affected / exposed	1 / 49 (2.04%)	3 / 49 (6.12%)	
occurrences (all)	2	3	
Eye irritation			

subjects affected / exposed	0 / 49 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	5	
Iris transillumination defect			
subjects affected / exposed	2 / 49 (4.08%)	3 / 49 (6.12%)	
occurrences (all)	4	3	
Photopsia			
subjects affected / exposed	3 / 49 (6.12%)	0 / 49 (0.00%)	
occurrences (all)	5	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 49 (6.12%)	3 / 49 (6.12%)	
occurrences (all)	3	4	
Anxiety			
subjects affected / exposed	3 / 49 (6.12%)	2 / 49 (4.08%)	
occurrences (all)	3	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 49 (6.12%)	9 / 49 (18.37%)	
occurrences (all)	3	11	
COVID-19			
subjects affected / exposed	2 / 49 (4.08%)	5 / 49 (10.20%)	
occurrences (all)	2	5	
Influenza			
subjects affected / exposed	2 / 49 (4.08%)	3 / 49 (6.12%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2017	Amendment number 2, dated 25 September 2017 reiterates the changes made in amendment 1. Main change included the modification of the population used for the primary efficacy analysis from the modified Intent-to-Treat (mITT) to the ITT population requested by the FDA
16 July 2019	Main changes included the updated of the primary efficacy timepoint which was extended from Year 1 (Week 52) to Year 1.5 (Week 78) based on preliminary results of the study, and addition of quality of life assessments (VFQ-25 and SF-36v2) at Visit 12 (Year 1.5)
23 December 2019	Main change included the extension of the follow-up period from 2 years to 5 years

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 reported

Notes: