Clinical trial results:
EXPLORE: A Phase 2, outcomes assessor-masked, multicentre, randomised study to evaluate the safety and efficacy of two doses of GT005 administered as a single subretinal injection in subjects with geographic atrophy secondary to age-related macular degeneration.

Summary

EudraCT number	2019-003421-22
Trial protocol	GB FR DE ES IE NL
Global end of trial date	05 April 2024

Results information

Result version number	v1 (current)
This version publication date	30 March 2025
First version publication date	30 March 2025

Trial information

Trial identification

Sponsor protocol code	GT005-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04437368
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Code II: CPPY988A12202

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	05 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of GT005 on the progression of GA in subjects with GA due to AMD.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 2019
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	Australia: 4
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United States: 68
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)	0
Adults (18-64 years)	8
From 65 to 84 years	79
85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were enrolled at 32 centers in 6 countries: 1 center in Australia, 3 centers in France, 2 centers in Germany, 5 centers in Spain, 3 centers in United Kingdom, and 18 centers in United States. A total of 98 subjects were enrolled into the study.

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	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	GT005 Low Dose [2E10 vg]

Arm description:

GT005 Low Dose [2E10 vg]

Arm type	Experimental
Investigational medicinal product name	GT005
Investigational medicinal product code	PPY988
Other name	PPY988
Pharmaceutical forms	Solution for injection
Routes of administration	Ophthalmic use

Dosage and administration details:

single time subretinal injection of GT005 [5E10 vg]

Arm title	GT005 High Dose [2E11 vg]

Arm description:

GT005 High Dose [2E11 vg]

Arm type	Experimental
Investigational medicinal product name	GT005
Investigational medicinal product code	PPY988
Other name	PPY988
Pharmaceutical forms	Solution for injection
Routes of administration	Ophthalmic use

Dosage and administration details:

single time subretinal injection of GT005 [2E11 vg]

Arm title	Untreated control

Arm description:

Subjects allocated to the untreated control group did not receive any treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control
Started	52	9	37
Randomized Part 1	10	9	14
Randomized Part 2	42	0 [1]	23
Randomized and treated Part 1	9	9	0 [2]
Randomized and treated Part 2	18	0 [3]	0 [4]
Completed	6	8	7
Not completed	46	1	30
Adverse event, serious fatal	3	-	2
Consent withdrawn by subject	4	-	3
Study terminated by sponsor	16	1	25
Sponsor instructions	23	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The disposition is broken down to greater detail: Randomized Part 1 , Randomized Part 2, Randomized and treated Part 1, and Randomized and treated Part 2.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The disposition is broken down to greater detail: Randomized Part 1 , Randomized Part 2, Randomized and treated Part 1, and Randomized and treated Part 2.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The disposition is broken down to greater detail: Randomized Part 1 , Randomized Part 2, Randomized and treated Part 1, and Randomized and treated Part 2.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The disposition is broken down to greater detail: Randomized Part 1 , Randomized Part 2, Randomized and treated Part 1, and Randomized and treated Part 2.

Baseline characteristics

Reporting groups	
Reporting group title	GT005 Low Dose [2E10 vg]
Reporting group description: GT005 Low Dose [2E10 vg]	
Reporting group title	GT005 High Dose [2E11 vg]
Reporting group description: GT005 High Dose [2E11 vg]	
Reporting group title	Untreated control
Reporting group description: Subjects allocated to the untreated control group did not receive any treatment.	

Reporting group values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control
Number of subjects	52	9	37
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	1	5
From 65-84 years	42	7	30
85 years and over	8	1	2
Age Continuous Units: years			
arithmetic mean	76.8	72.7	75.2
standard deviation	± 7.33	± 8.96	± 7.07
Sex: Female, Male Units: Participants			
Female	34	5	18
Male	18	4	19
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	51	7	35
More than one race	0	0	0
Unknown or Not Reported	0	2	2

Reporting group values	Total		
Number of subjects	98		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	8		
From 65-84 years	79		
85 years and over	11		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	57		
Male	41		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	93		
More than one race	0		
Unknown or Not Reported	4		

End points

End points reporting groups	
Reporting group title	GT005 Low Dose [2E10 vg]
Reporting group description: GT005 Low Dose [2E10 vg]	
Reporting group title	GT005 High Dose [2E11 vg]
Reporting group description: GT005 High Dose [2E11 vg]	
Reporting group title	Untreated control
Reporting group description: Subjects allocated to the untreated control group did not receive any treatment.	

Primary: The change from baseline to Week 48 in geographic atrophy (GA) - Part 1	
End point title	The change from baseline to Week 48 in geographic atrophy (GA) - Part 1
End point description: The change from baseline to Week 48 in GA area as measured by fundus autofluorescence (FAF)	
End point type	Primary
End point timeframe: Baseline, Weeks 12, 24, 36, and 48	

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	12	
Units: mm2				
least squares mean (standard error)				
Part 1 Week 12 (n=9,8,12)	0.773 (± 0.2151)	0.764 (± 0.2159)	0.482 (± 0.1848)	
Part 1 Week 24 (n=9,7,9)	1.338 (± 0.2763)	1.519 (± 0.2845)	0.680 (± 0.2500)	
Part 1 Week 36 (n=6,7,10)	1.800 (± 0.3740)	2.044 (± 0.3669)	1.132 (± 0.3229)	
Part 1 Week 48 (n=5,8,10)	2.120 (± 0.3726)	2.378 (± 0.3414)	1.144 (± 0.3040)	

Statistical analyses

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 12	
Comparison groups	Untreated control v GT005 Low Dose [2E10 vg]

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.291
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.195
upper limit	0.777
Variability estimate	Standard error of the mean
Dispersion value	0.2838

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 12	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.282
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.206
upper limit	0.769
Variability estimate	Standard error of the mean
Dispersion value	0.2843

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 24	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.658

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.017
upper limit	1.299
Variability estimate	Standard error of the mean
Dispersion value	0.373

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 24	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.189
upper limit	1.49
Variability estimate	Standard error of the mean
Dispersion value	0.3791

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 36	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.912
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.078
upper limit	1.746
Variability estimate	Standard error of the mean
Dispersion value	0.4887

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 36	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.668
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.177
upper limit	1.512
Variability estimate	Standard error of the mean
Dispersion value	0.4954

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 48	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	0.976
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.15
upper limit	1.803
Variability estimate	Standard error of the mean
Dispersion value	0.4813

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 48	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	1.233
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.445
upper limit	2.022
Variability estimate	Standard error of the mean
Dispersion value	0.4573

Secondary: The change from baseline in geographic atrophy (GA) at Week 72 and Week 96 - Part 1

End point title	The change from baseline in geographic atrophy (GA) at Week 72 and Week 96 - Part 1
End point description:	
The change from baseline to Week 48 in GA area as measured by fundus autofluorescence (FAF)	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 72 and 96	

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	9	
Units: mm2				
least squares mean (standard error)				
Part 1 Week 72 (n=5,7,9)	3.643 (± 0.9725)	3.149 (± 0.9150)	1.875 (± 0.8273)	
Part 1 Week 96 (n=6,8,7)	4.837 (± 1.0712)	4.074 (± 1.0305)	2.796 (± 0.9240)	

Statistical analyses

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description:	
Week 72	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	1.769
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.441
upper limit	3.979
Variability estimate	Standard error of the mean
Dispersion value	1.2808

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 72	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	1.274
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.863
upper limit	3.412
Variability estimate	Standard error of the mean
Dispersion value	1.2349

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 96	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	2.041

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.386
upper limit	4.468
Variability estimate	Standard error of the mean
Dispersion value	1.4177

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description:	
Week 96	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean
Point estimate	1.278
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.099
upper limit	3.655
Variability estimate	Standard error of the mean
Dispersion value	1.3857

Secondary: Summary of Adverse Events

End point title	Summary of Adverse Events

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a subject or clinical investigation subject.

A TEAE is defined as any AE that develops after randomization or any AE already present that worsens following randomization. The primary
summaries of AEs are based on TEAEs.

AE = adverse event
SAE = serious adverse event
Rel = related
Trt = study treatment
Proc. = procedure
Disc. = discontinuation
AESI = AE of special interest
Surg. = surgical

End point type	Secondary

End point timeframe:

Adverse events are reported from randomization to the end of study, at Week 96, up to a maximum timeframe of approximately 96 weeks.

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	9	37	
Units: Participants				
Subjects with at least 1 ocular AE - study eye	18	9	2	
Subjects with at least 1ocular AE - fellow eye	6	3	5	
Subjects with at least one non-ocular AE	13	8	14	
n >= 1 ocular AE rel. to trt. - study eye	3	4	0	
n with at least 1 non-ocular AE rel. to trt.	0	0	0	
n >= 1 ocular AE rel. to surg proc - study eye	12	7	0	
n >= 1 non-ocular AE rel. to surg. proc.	0	0	0	
n >= 1 ocular AE rel.to proc.- study eye	1	1	0	
n >= 1 non-ocular AE rel. to study proc.	1	0	0	
n >= 1 ocular AE leading to disc.- study eye	0	0	0	
n >= 1 non-ocular AE leading to disc.	3	0	2	
n >= 1 ocular AESI for the study eye	4	7	0	
n with at least 1 ocular AESI for the fellow eye	0	0	1	
n with at least 1 ocular SAE for the study eye	1	0	0	
n with at least 1 ocular SAE for the fellow eye	0	0	0	
Subjects with at least 1 non-ocular SAE	5	2	4	
n >= 1 ocular SAE rel. to study trt.- study eye	0	0	0	
n >= 1 non-ocular SAE rel.to study trt.	0	0	0	
n >= 1 ocular SAE rel. to surg. proc. - study eye	0	0	0	
n >= 1 non-ocular SAE rel.to surg. proc.	0	0	0	
n >= 1 ocular SAE rel. to study proc. - study eye	0	0	0	
n >= 1 non-ocular SAE rel. to study proc.	0	0	0	
n >= 1 ocular SAE leading to disc.- study eye	0	0	0	
n >= 1 non-ocular SAE leading to study disc.	3	0	2	
Deaths	3	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Ocular adverse events by primary system organ class and preferred

term for the study eye

End point title	Ocular adverse events by primary system organ class and preferred term for the study eye

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a subject or clinical investigation subject.

A TEAE is defined as any AE that develops after randomization or any AE already present that worsens following randomization. The primary
summaries of AEs are based on TEAEs.

System organ classes are sorted alphabetically, and preferred terms are sorted by decreasing overall frequency within system organ class.

End point type	Secondary

End point timeframe:

Adverse events are reported from randomization to the end of study, at Week 96, up to a maximum timeframe of approximately 96 weeks.

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	9	37	
Units: Participants				
Subjects with at least one event	18	9	2	
Eye disorders	15	9	2	
-Retinal pigmentation	3	6	0	
-Conjunctival haemorrhage	6	1	0	
-Cataract	3	2	1	
-Cataract nuclear	2	1	0	
-Eye pain	1	2	0	
-Retinal haemorrhage	2	1	0	
-Anterior chamber cell	1	1	0	
-Blepharitis	2	0	0	
-Conjunctivitis allergic	1	1	0	
-Anterior chamber flare	0	1	0	
-Choroidal detachment	0	1	0	
-Conjunctival hyperaemia	1	0	0	
-Dry eye	1	0	0	
-Eye pruritus	0	0	1	
-Hypotony maculopathy	0	1	0	
-Iridocyclitis	0	1	0	
-Iritis	1	0	0	
-Keratitis	1	0	0	
-Lacrimation increased	0	1	0	
-Macular hole	1	0	0	
-Meibomian gland dysfunction	1	0	0	
-Metamorphopsia	1	0	0	
-Ocular hypertension	1	0	0	
-Open angle glaucoma	0	1	0	
-Photophobia	0	1	0	
-Photopsia	1	0	0	

-Posterior capsule opacification	0	0	1	
-Punctate keratitis	1	0	0	
-Retinal depigmentation	1	0	0	
-Visual acuity reduced	1	0	0	
-Visual impairment	1	0	0	
-Visual snow syndrome	1	0	0	
-Vitreous floaters	1	0	0	
-Vitreous haemorrhage	1	0	0	
Injury, poisoning and procedural complications	4	1	0	
-Post procedural discomfort	2	0	0	
-Procedural pain	1	1	0	
-Suture related complication	1	1	0	
Investigations	4	3	0	
-Intraocular pressure increased	4	3	0	
Skin and subcutaneous tissue disorders	1	0	0	
-Telangiectasia	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Non-ocular adverse events - summary

End point title	Non-ocular adverse events - summary

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a subject or clinical investigation subject.

A TEAE is defined as any AE that develops after randomization or any AE already present that worsens following randomization. The primary
summaries of AEs are based on TEAEs.

End point type	Secondary

End point timeframe:

Adverse events are reported from randomization to the end of study, at Week 96, up to a maximum timeframe of approximately 96 weeks.

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	9	37	
Units: Participants	13	8	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in GA morphology from Baseline to Week 96 on colour fundus photography (CFP) - Number of participants with increase in Fundus autofluorescence - Part 1

End point title	Change in GA morphology from Baseline to Week 96 on colour fundus photography (CFP) - Number of participants with increase in Fundus autofluorescence - Part 1

End point description:

Change in GA morphology on multimodal imaging through Week 96

End point type	Secondary

End point timeframe:

Baseline, Weeks 5,12,24,36,48,72,96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	12	
Units: Participants				
Part 1 Week 5 (n= 0,2,0)	999	2	999	
Part 1 Week 12 (n=9,8,12)	8	8	11	
Part 1 Week 24 (n=9,7,10)	8	7	10	
Part 1 Week 36 (n=6,7,10)	5	7	10	
Part 1 Week 48 (n=5,8,10)	5	8	10	
Part 1 Week 72 (n=5,8,9)	5	8	9	
Part 1 Week 96 (n=6,8,7)	6	8	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 48 in GA morphology on colour fundus photography (CFP) - Number of participants with increase in Fundus autofluorescence - Part 2

End point title	Change from Baseline to Week 48 in GA morphology on colour fundus photography (CFP) - Number of participants with increase in Fundus autofluorescence - Part 2

End point description:

Change in GA morphology on multimodal imaging through Week 48

End point type	Secondary

End point timeframe:

Baseline, Weeks 5,12,24,36,48

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	0[1]	20	
Units: Participants				
Part 2 Week 5 (n= 16,0, 0)	16		999	
Part 2 Week 12 (n=17,0,20)	17		20	
Part 2 Week 24 (n=17,0,11)	16		11	
Part 2 Week 36 (n=14,0,0)	13		999	
Part 2 Week 48 (n=5,0,0)	5		999	

Notes:

[1] - Not applicable for Part 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Best corrected visual acuity (BCVA) Score from Baseline through Week 96 via the early treatment for diabetic retinopathy (ETDRS) chart - Part 1

End point title	Change in Best corrected visual acuity (BCVA) Score from Baseline through Week 96 via the early treatment for diabetic retinopathy (ETDRS) chart - Part 1

End point description:

BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts.

Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 5, 8, 12, 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	12	
Units: Letters read				
least squares mean (standard error)				
Part 1 - Week 1 (n=9,9,0)	-4.7 (± 4.04)	-5.2 (± 4.27)	999 (± 999)	
Part 1 - Week 5 (n=8,9,0)	-1.7 (± 4.08)	-7.6 (± 4.26)	999 (± 999)	
Part 1 - Week 8 (n=9,9,0)	-1.6 (± 4.03)	-4.5 (± 4.23)	999 (± 999)	
Part 1 - Week 12 (N=9,9,12)	-2.3 (± 4.03)	-7.5 (± 4.18)	-1.2 (± 3.81)	
Part 1 - Week 24 (n=9,9,10)	-5.6 (± 4.03)	-12.0 (± 4.18)	-0.4 (± 3.87)	
Part 1 - Week 36 (n=8,8,10)	-10.0 (± 4.10)	-12.9 (± 4.28)	-1.0 (± 3.89)	
Part 1 - Week 48 (n=5,8,10)	-8.6 (± 4.52)	-13.3 (± 4.32)	-5.7 (± 3.91)	
Part 1 - Week 72 (n=5,8,10)	-6.3 (± 4.56)	-9.6 (± 4.34)	-8.9 (± 3.94)	
Part 1 - Week 96 (n=6,8,7)	-6.5 (± 4.50)	-11.0 (± 4.33)	-7.9 (± 4.30)	

Statistical analyses

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description:	
Week 12	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.3
upper limit	8.1
Variability estimate	Standard error of the mean
Dispersion value	5.49

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description:	
Week 12	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-6.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.3
upper limit	3.7
Variability estimate	Standard error of the mean
Dispersion value	5.96

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description:	
Week 24	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-5.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.5
upper limit	4.1
Variability estimate	Standard error of the mean
Dispersion value	5.54

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 24	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-11.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.7
upper limit	-1.6
Variability estimate	Standard error of the mean
Dispersion value	6

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 36	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-9

Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.4
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	5.63

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 36	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-11.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.1
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	6.08

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 48	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-2.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.7
upper limit	6.9
Variability estimate	Standard error of the mean
Dispersion value	5.88

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 48	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-7.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.9
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	6.14

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 72	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	2.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.4
upper limit	12.5
Variability estimate	Standard error of the mean
Dispersion value	5.96

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 72	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.1
upper limit	9.6
Variability estimate	Standard error of the mean
Dispersion value	6.18

Statistical analysis title	GT005 Low Dose [2E10 vg] v Untreated control
Statistical analysis description: Week 96	
Comparison groups	GT005 Low Dose [2E10 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	1.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.7
upper limit	11.5
Variability estimate	Standard error of the mean
Dispersion value	6.07

Statistical analysis title	GT005 High Dose [2E11 vg] v Untreated control
Statistical analysis description: Week 96	
Comparison groups	GT005 High Dose [2E11 vg] v Untreated control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
Method	mixed model repeated measures
Parameter estimate	LS Mean Difference
Point estimate	-3

Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.8
upper limit	7.8
Variability estimate	Standard error of the mean
Dispersion value	6.47

Secondary: Change in Low luminance difference (LLD) letter count from Baseline at Weeks 12, 24, 36, 48, 72 and 96, via early treatment for diabetic retinopathy (ETDRS) chart - part 1

End point title	Change in Low luminance difference (LLD) letter count from Baseline at Weeks 12, 24, 36, 48, 72 and 96, via early treatment for diabetic retinopathy (ETDRS) chart - part 1

End point description:

LLD was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts.

The test was to be performed after BCVA testing, prior to pupil dilation, and distance refraction was to be carried out before Low Luminance Visual Acuity (LLVA) was measured.

LLVA was to be measured by placing a 2.0-log-unit neutral density filter over the front of each eye and having the subject read the normally illuminated ETDRS chart. The LLD was calculated as the difference between BCVA and LLVA.

Initially, letters were to be read at a distance of 4 metres from the chart. If <20 letters were read at 4 metres, testing at 1 metre should have been performed. LLD was to be reported as number of letters read correctly by the subject.

Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	12	
Units: Letters read				
arithmetic mean (standard deviation)				
Part 1 - Week 12 (N=9,9,12)	2.0 (± 9.06)	2.4 (± 22.49)	-2.0 (± 7.21)	
Part 1 - Week 24 (n=9,9,10)	2.1 (± 8.40)	2.9 (± 24.81)	-2.9 (± 7.68)	
Part 1 - Week 36 (n=8,8,10)	2.3 (± 15.65)	-7.5 (± 19.41)	-4.0 (± 12.51)	
Part 1 - Week 48 (n=5,8,10)	3.0 (± 6.96)	1.8 (± 26.25)	-6.2 (± 19.99)	
Part 1 - Week 72 (n=5,8,10)	4.4 (± 7.57)	3.1 (± 32.24)	-6.6 (± 21.15)	
Part 1 - Week 96 (n=6,8,6)	5.2 (± 8.47)	1.5 (± 29.17)	-10.5 (± 27.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Low luminance difference (LLD) letter count from Baseline at Weeks 12, 24, 36, and 48, via early treatment for diabetic retinopathy (ETDRS) chart - part 2

End point title	Change in Low luminance difference (LLD) letter count from Baseline at Weeks 12, 24, 36, and 48, via early treatment for diabetic retinopathy (ETDRS) chart - part 2

End point description:

LLD was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts.

The test was to be performed after BCVA testing, prior to pupil dilation, and distance refraction was to be carried out before Low Luminance Visual Acuity (LLVA) was measured.

LLVA was to be measured by placing a 2.0-log-unit neutral density filter over the front of each eye and having the subject read the normally illuminated ETDRS chart. The LLD was calculated as the difference between BCVA and LLVA.

Initially, letters were to be read at a distance of 4 metres from the chart. If <20 letters were read at 4 metres, testing at 1 metre should have been performed. LLD was to be reported as number of letters read correctly by the subject.

Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24, 36, and 48

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	0[2]	20	
Units: Letters read				
arithmetic mean (standard deviation)				
Part 2 - Week 12 (N=18,0,20)	0.7 (± 10.83)	()	-1.4 (± 11.76)	
Part 2 - Week 24 (n=17,0,10)	2.6 (± 9.98)	()	-1.6 (± 20.13)	
Part 2 - Week 36 (n=14,0,0)	4.6 (± 11.77)	()	999 (± 999)	
Part 2 - Week 48 (n=5,0,0)	-2.8 (± 4.32)	()	999 (± 999)	

Notes:

[2] - Not applicable for Part 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Weeks 24, 36, 48, 72 and 96 in Reading performance, measured as the maximum reading speed (words per minute), as assessed by Minnesota low-vision reading test (MNRead) chart - part 1

End point title	Change from Baseline at Weeks 24, 36, 48, 72 and 96 in Reading performance, measured as the maximum reading speed (words per minute), as assessed by Minnesota low-vision reading test (MNRead) chart - part 1

End point description:

The maximum reading speed (MRS) represents the highest reading speed an individual can achieve when print size is not a limiting factor. Essentially, it measures how quickly a person can read text when the print is large enough to be easily readable.

A higher count represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	9	
Units: Words read per minute				
arithmetic mean (standard deviation)				
Part 1 - Week 24 (n=9,8,9)	20.384 (± 74.7769)	-36.154 (± 40.3322)	-7.837 (± 21.8918)	
Part 1 - Week 36 (n=7,7,8)	-15.048 (± 33.0479)	-34.653 (± 27.2693)	-15.245 (± 22.0983)	
Part 1 - Week 48 (n=4,7,9)	10.397 (± 11.8698)	-36.285 (± 40.0938)	-6.837 (± 31.6162)	
Part 1 - Week 72 (n=5,7,9)	-20.796 (± 42.2571)	-44.913 (± 46.7594)	-15.429 (± 30.1012)	
Part 1 - Week 96 (n=6,5,5)	10.802 (± 32.1161)	-32.266 (± 36.9172)	-21.602 (± 26.0643)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Weeks 24, 36 and 48 in Reading performance, measured as the maximum reading speed (words per minute), as assessed by Minnesota low-vision reading test (MNRead) chart - part 2

End point title	Change from Baseline at Weeks 24, 36 and 48 in Reading performance, measured as the maximum reading speed (words per minute), as assessed by Minnesota low-vision reading test (MNRead) chart - part 2

End point description:

A higher count represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36 and 48

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	0[3]	10	
Units: Words read per minute				
arithmetic mean (standard deviation)				
Part 2 - Week 24 (n=16,0,10)	15.581 (± 78.2848)	()	-30.707 (± 27.3225)	
Part 2 - Week 36 (n=14,0,0)	9.812 (± 94.4255)	()	999 (± 999)	
Part 2 - Week 48 (n=5,0,0)	-28.111 (± 38.6209)	()	999 (± 999)	

Notes:

[3] - Not applicable for Part 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Weeks 24, 36, 48, 72 and 96 in Functional reading independence (FRI) index - part 1

End point title	Change from Baseline at Weeks 24, 36, 48, 72 and 96 in Functional reading independence (FRI) index - part 1

End point description:

The FRI index is a patient-reported outcome measure developed specifically for use in GA patients. The FRI index evaluates the level of independence subjects have in performing everyday activities that require reading, such as writing a cheque or reading a prescription. Scores derived from the index range from 1 (unable to do) to 4 (total independence).

A higher score represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	10	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Part 1 - Week 24 (n=9,8,10)	0.7 (± 3.57)	-1.3 (± 2.55)	-0.3 (± 4.06)	
Part 1 - Week 36 (n=8,5,10)	-1.0 (± 4.24)	2.6 (± 4.10)	-0.6 (± 4.72)	
Part 1 - Week 48 (n=6,7,10)	0.5 (± 2.43)	-0.1 (± 7.69)	-3.4 (± 4.38)	
Part 1 - Week 72 (n=5,7,10)	-3.8 (± 4.60)	0.4 (± 3.41)	-1.3 (± 4.35)	
Part 1 - Week 96 (n=6,6,7)	-2.7 (± 5.79)	-2.0 (± 3.29)	-0.7 (± 5.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Weeks 24, 36 and 48 in Functional reading independence (FRI) index - part 2

End point title	Change from Baseline at Weeks 24, 36 and 48 in Functional reading independence (FRI) index - part 2

End point description:

The FRI index is a patient-reported outcome measure developed specifically for use in GA patients. The FRI index evaluates the level of independence subjects have in performing everyday activities that require reading, such as writing a cheque or reading a prescription. Scores derived from the index range from 1 (unable to do) to 4 (total independence).

A higher score represents better visual functioning.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36 and 48

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	0[4]	9	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Part 2 - Week 24 (n=17,0,9)	-0.4 (± 2.83)	()	0.4 (± 6.86)	
Part 2 - Week 36 (n=14,0,0)	-1.7 (± 3.83)	()	999 (± 999)	
Part 2 - Week 48 (n=5,0,0)	0.4 (± 5.13)	()	999 (± 999)	

Notes:

[4] - Not applicable for Part 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Weeks 24, 36, 48, 72 and 96 in Patient Reported Outcomes (Visual Function Questionnaire-25) - Composite Score - Part 1

End point title	Change From Baseline at Weeks 24, 36, 48, 72 and 96 in Patient Reported Outcomes (Visual Function Questionnaire-25) - Composite Score - Part 1

End point description:

The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains.

The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. A composite score is derived based on the average of the 11 subscales.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	10	
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Part 1 - Week 24 (n=9,9,10)	-2.312 (± 5.7079)	-3.755 (± 7.4470)	-7.304 (± 12.5136)	
Part 1 - Week 36 (n=8,6,10)	-4.400 (± 11.1307)	1.960 (± 9.0113)	-4.706 (± 11.8617)	
Part 1 - Week 48 (n=6,8,10)	-6.439 (± 24.2128)	-6.810 (± 11.5980)	-4.091 (± 15.3598)	
Part 1 - Week 72 (n=5,8,10)	-8.698 (± 22.1289)	-3.332 (± 8.1470)	-3.826 (± 11.0029)	
Part 1 - Week 96 (n=6,7,7)	-10.352 (± 23.9470)	0.171 (± 11.3543)	-10.700 (± 11.6900)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Weeks 24, 36, 48, 72 and 96 in Patient Reported Outcomes (Visual Function Questionnaire-25) - Composite Score - Part 2

End point title	Change From Baseline at Weeks 24, 36, 48, 72 and 96 in Patient Reported Outcomes (Visual Function Questionnaire-25) - Composite Score - Part 2

End point description:

The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains.

The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. A composite score is derived based on the average of the 11 subscales.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 36, 48, 72 and 96

End point values	GT005 Low Dose [2E10 vg]	GT005 High Dose [2E11 vg]	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	0[5]	8	
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Part 2 - Week 24 (n=17,0,8)	-4.034 (± 6.8881)	()	-3.070 (± 7.4251)	
Part 2 - Week 36 (n=14,0,0)	-2.733 (± 7.9219)	()	999 (± 999)	
Part 2 - Week 48 (n=5,0,0)	-0.530 (± 6.9722)	()	999 (± 999)	

Notes:
[5] - Not applicable for Part 2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are reported from randomization to the end of study, at Week 96, up to a maximum timeframe of approximately 96 weeks.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	GT005@High dose@[2E11 vg]

Reporting group description:

GT005@High dose@[2E11 vg]

Reporting group title	GT005@Low dose@[2E10 vg]

Reporting group description:

GT005@Low dose@[2E10 vg]

Reporting group title	Overall

Reporting group description:

Overall

Reporting group title	Untreated control

Reporting group description:

Untreated control

Serious adverse events	GT005@High dose@[2E11 vg]	GT005@Low dose@[2E10 vg]	Overall
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	5 / 52 (9.62%)	11 / 98 (11.22%)
number of deaths (all causes)	0	3	5
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

Lung neoplasm malignant			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung adenocarcinoma stage IV			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Sciatica			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual acuity reduced - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Choking			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Staphylococcal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Untreated control		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cancer			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Lung neoplasm malignant			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung adenocarcinoma stage IV			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Sciatica			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual acuity reduced - Study eye			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Choking			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	GT005@High dose@[2E11 vg]	GT005@Low dose@[2E10 vg]	Overall
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	19 / 52 (36.54%)	44 / 98 (44.90%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer recurrent			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Meningioma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	2 / 98 (2.04%)
occurrences (all)	1	0	2
Orthostatic hypotension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Peripheral ischaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Drug intolerance			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Investigations			
Blood potassium decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Intraocular pressure increased - Study eye			
subjects affected / exposed	3 / 9 (33.33%)	4 / 52 (7.69%)	7 / 98 (7.14%)
occurrences (all)	4	5	9
C-reactive protein increased			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	0	1	2
Blood pressure increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	2	2
Blood pressure decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Lower limb fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Joint dislocation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	3 / 98 (3.06%)
occurrences (all)	1	2	4
Ligament sprain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Suture related complication - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Tendon rupture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Lumbar vertebral fracture			

subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Meniscus injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Post procedural discomfort - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	2 / 98 (2.04%)
occurrences (all)	0	2	2
Procedural pain - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Skin abrasion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Upper limb fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Coronary artery disease			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Cognitive disorder			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Tension headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Seizure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Hemiparesis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	0	1	2
Facial paralysis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Transient ischaemic attack			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Anaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	2 / 98 (2.04%)
occurrences (all)	1	0	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Eye disorders			

Anterior chamber flare - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Anterior chamber cell - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Cataract - Fellow eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	3 / 98 (3.06%)
occurrences (all)	1	0	3
Blepharitis - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	2 / 98 (2.04%)
occurrences (all)	0	2	2
Blepharitis - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	2 / 52 (3.85%)	2 / 98 (2.04%)
occurrences (all)	0	2	2
Cataract - Study eye			
subjects affected / exposed	2 / 9 (22.22%)	3 / 52 (5.77%)	6 / 98 (6.12%)
occurrences (all)	2	3	6
Cataract nuclear - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	2 / 52 (3.85%)	3 / 98 (3.06%)
occurrences (all)	2	2	4
Choroidal detachment - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Choroidal neovascularisation - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Conjunctival haemorrhage - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	6 / 52 (11.54%)	7 / 98 (7.14%)
occurrences (all)	1	6	7
Conjunctivitis allergic - Fellow eye			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Conjunctival hyperaemia - Study eye			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Conjunctivitis allergic - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Iridocyclitis - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Hypotony maculopathy - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Eye pruritus - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Eye pruritus - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Eye pain - Study eye			
subjects affected / exposed	2 / 9 (22.22%)	1 / 52 (1.92%)	3 / 98 (3.06%)
occurrences (all)	2	1	3
Dry eye - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Dry eye - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Iritis - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Meibomian gland dysfunction - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Macular hole - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1

Lacrimation increased - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Keratitis - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Meibomian gland dysfunction - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Metamorphopsia - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Ocular hypertension - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Open angle glaucoma - Fellow eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Photopsia - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Photopsia - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Photophobia - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Open angle glaucoma - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Posterior capsule opacification - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Retinal degeneration - Fellow eye			

subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Punctate keratitis - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Posterior capsule opacification - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Retinal depigmentation - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Retinal haemorrhage - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Retinal haemorrhage - Study eye			
subjects affected / exposed	1 / 9 (11.11%)	2 / 52 (3.85%)	3 / 98 (3.06%)
occurrences (all)	1	2	3
Retinal oedema - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Visual snow syndrome - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Visual impairment - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Visual impairment - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Retinal tear - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Retinal pigmentation - Study eye			
subjects affected / exposed	6 / 9 (66.67%)	3 / 52 (5.77%)	9 / 98 (9.18%)
occurrences (all)	6	3	9

Vitreous haemorrhage - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Vitreous floaters - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Vitreous floaters - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Vitreous detachment - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	2 / 98 (2.04%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	2 / 98 (2.04%)
occurrences (all)	0	0	2
Diverticulum intestinal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Umbilical hernia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Oesophageal achalasia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Loose tooth			

subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Inguinal hernia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Rosacea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Telangiectasia - Study eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	2	2
Urticaria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Telangiectasia - Fellow eye			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	2	2
Renal and urinary disorders			
Urethral polyp			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Urethral haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Renal impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Spinal osteoarthritis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	0	1	2
Rotator cuff syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Plantar fasciitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Osteoarthritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Muscle contracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	2	2
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
COVID-19			
subjects affected / exposed	2 / 9 (22.22%)	3 / 52 (5.77%)	6 / 98 (6.12%)
occurrences (all)	2	3	6
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 52 (1.92%)	2 / 98 (2.04%)
occurrences (all)	1	1	2
Herpes zoster			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1

Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 52 (0.00%)	2 / 98 (2.04%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1
Obesity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 52 (0.00%)	1 / 98 (1.02%)
occurrences (all)	0	0	1
Dyslipidaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 52 (1.92%)	1 / 98 (1.02%)
occurrences (all)	0	1	1

Non-serious adverse events	Untreated control		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 37 (43.24%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer recurrent			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Meningioma			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Orthostatic hypotension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Peripheral ischaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Drug intolerance subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Investigations Blood potassium decreased subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Intraocular pressure increased - Study eye subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
C-reactive protein increased subjects affected / exposed occurrences (all)	 1 / 37 (2.70%) 1		
Blood pressure increased subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Blood pressure decreased subjects affected / exposed occurrences (all)	 1 / 37 (2.70%) 1		
Injury, poisoning and procedural complications			

Contusion				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Lower limb fracture				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Joint dislocation				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Hand fracture				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Fall				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Ligament sprain				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Suture related complication - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Tendon rupture				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Lumbar vertebral fracture				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Meniscus injury				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Muscle strain				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Post procedural discomfort - Study eye				

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Procedural pain - Study eye subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Skin abrasion subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Skin laceration subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Upper limb fracture subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Cardiac disorders			
Cardiomyopathy subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Coronary artery disease subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Nervous system disorders			
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Tension headache subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Seizure subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Hemiparesis			

subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Facial paralysis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Transient ischaemic attack			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Eye disorders			
Anterior chamber flare - Study eye			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Anterior chamber cell - Study eye			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Cataract - Fellow eye			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Blepharitis - Study eye			

subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Blepharitis - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Cataract - Study eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Cataract nuclear - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Choroidal detachment - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Choroidal neovascularisation - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Conjunctival haemorrhage - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Conjunctivitis allergic - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Conjunctival hyperaemia - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Conjunctivitis allergic - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Iridocyclitis - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Hypotony maculopathy - Study eye				

subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Eye pruritus - Study eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Eye pruritus - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Eye pain - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Dry eye - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Dry eye - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Iritis - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Meibomian gland dysfunction - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Macular hole - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Lacrimation increased - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Keratitis - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Meibomian gland dysfunction - Study eye				

subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Metamorphopsia - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Ocular hypertension - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Open angle glaucoma - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Photopsia - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Photopsia - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Photophobia - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Open angle glaucoma - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Posterior capsule opacification - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Retinal degeneration - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Punctate keratitis - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Posterior capsule opacification - Study eye				

subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Retinal depigmentation - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Retinal haemorrhage - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Retinal haemorrhage - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Retinal oedema - Fellow eye				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Visual snow syndrome - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Visual impairment - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Visual impairment - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Retinal tear - Fellow eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Retinal pigmentation - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Vitreous haemorrhage - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Vitreous floaters - Study eye				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Vitreous floaters - Fellow eye				

subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Vitreous detachment - Fellow eye			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Diverticulum intestinal			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Umbilical hernia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Oesophageal achalasia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Loose tooth			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Inguinal hernia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rosacea			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Telangiectasia - Study eye			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Telangiectasia - Fellow eye			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Urethral polyp			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Urethral haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Spinal osteoarthritis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Rotator cuff syndrome			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Plantar fasciitis			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Muscle contracture subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Temporomandibular joint syndrome subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
COVID-19 subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Bronchitis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Ear infection subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Herpes zoster subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Sinusitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Metabolism and nutrition disorders Vitamin D deficiency			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Obesity			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Dyslipidaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 October 2019	The protocol was updated to extricate that the primary endpoint was masked to the assessor and the number of subjects had been increased to include a projected 10% withdrawal rate
13 May 2020	The protocol was updated to change the corticosteroid regimen required for GT005-treated subjects (from systemic to topical administration) given the COVID-19 risk, and also due to the absence of clinically meaningful inflammation in all dose escalation cohorts of the ongoing Phase I/II study, FOCUS. An additional in-clinic visit added at Week 8 (Visit 5) was included. The number of study subjects increased to adequately power for a statistically significant effect assuming the true underlying change in GA area was inhibited by a 40% treatment effect. Inclusion/Exclusion criteria were updated to more accurately reflect the anticipated age group of subjects with GA, to cap the number of subjects with GA lesion size >10 mm2, to clarify the serum CFI inclusion and to further specify the excluded confounding comorbidities. Given the low prevalence of CFI mutations and desired to minimize subject study activities, genotyping and serum CFI results received to confirm eligibility prior to other screening activities commencing. CNV was added to the list of adverse events of special interest.
13 November 2020	Subject participation period has been extended to a total of 96 weeks with the addition of 2 extra visits at Week 72 and Week 96. Key changes to the eligibility criteria included: • Subjects that have dry AMD and/or GA, secondary to AMD in study eye as determined by the Investigator, and a diagnosis of AMD in the contralateral eye (except if the subject is monocular) lowering of the BCVA score from 34 or better to 24 letters or better, using ETDRS charts. • included an evidence-based approach to enrolment of subjects into the study. • clarified the required duration of prior intraocular surgery before screening cataract surgery. • broadened the malignancies/cancer types excluded from the study. The addition of an aqueous sample for biomarker analysis at Visit 2 to facilitate understanding of long-term transgene expression. All OCT-bleb scans to be read by a dose-masked reader at the CRC. Inclusion of new imaging assessments: FA and OCT-A. The differing OCT modalities (OCT-A, OCT bleb and OCT macula) have been clarified, all OCT scans were sent to the CRC and that OCT bleb scans are to be read by a dose-masked reader at the CRC. A separate genotyping ICF was +created to facilitate ease of genotyping for screening eligibility. Randomisation to either study eye if both are eligible has been changed to select the worse eye (BVCA score). Removal of the requirement to identify the PRL prior to surgery. The location of the bleb has been relocated to outside the vascular arcades. Safety reporting requirements updated to collect all AEs from date of consent.

03 June 2021	Change in eligibility criteria to allow inclusion of subjects with CNV/wet AMD in fellow eye. Subjects with fellow eye CNV were stratified across all three treatment groups. Clarification of Screening CNV assessment with OCT-A and FA imaging requirements. Clarification of Microperimetry imaging requirements. Removal of text stating OCT-A certification was not required. Viral shedding statement updated to be consistent with core study documentation and text included to confirm viral shedding was monitored in the Phase I/II FOCUS study. Correction of text related to causality assessment of adverse events associated with surgical procedures rather than study procedures.
06 December 2022	The study design was amended to include two parts: Part 1 provides an evaluation of CFI rare variant GA subjects with the low and high dose of GT005 compared with untreated control, randomized in a 2:1 ratio; Part 2 evaluates the broad genetic GA population (including CFI rare variant) with the low dose of GT005 compared with untreated control randomized in a 2:1 ratio. The dosing and administration section was amended such that subretinal GT005 dosing occurred via one or more GT005 administration bleb(s). Prohibited Medications section: subjects should not receive systemic and/or locally in the study eye approved and investigational GA treatment up to Week 48 for the untreated group and until the end of study for the treated group. The overall study sample size increased to approximately 202 and the number investigational sites increased from 40 to approximately 60. Statistical Methods have been updated in line with the change in sample size and study design. Secondary and exploratory study endpoints have also been revised. RPE changes following GT005 treatment to be captured as an AESI. Additionally, information regarding recommendations for further safety-related functional assessments follow-up for affected subjects have been added to the protocol to align with the Central Imaging Manual.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: