Clinical trial results:
A Phase 2b Randomized, Double-masked, Controlled Trial to Establish the Safety and Efficacy of Zimura™ (Complement C5 Inhibitor) Compared to Sham in Subjects with Autosomal Recessive Stargardt Disease

Summary

EudraCT number	2017-004783-35
Trial protocol	DE GB HU ES IT
Global end of trial date	31 March 2025

Results information

Result version number	v1 (current)
This version publication date	27 March 2026
First version publication date	27 March 2026

Trial information

Trial identification

Sponsor protocol code	OPH2005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03364153
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development, Inc
Sponsor organisation address	1 Astellas Way, Northbrook, United States, 60062
Public contact	Clinical Transparency, Astellas Pharma Global Development, Inc, +1 800-888-7704, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Transparency, Astellas Pharma Global Development, Inc, +1 800-888-7704, astellas.resultsdisclosure@astellas.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	31 March 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the safety and efficacy of avacincaptad pegol (ACP) intravitreal injection compared to sham in participants with autosomal recessive Stargardt disease 1 (STGD1).

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the following:
- Declaration of Helsinki and CIOMS International Ethical Guidelines
- Applicable ICH GCP Guidelines
- Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 63
Worldwide total number of subjects	121
EEA total number of subjects	51

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)	121
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants of either gender, of 18 to 60 years of age (inclusive), with the diagnosis of autosomal recessive STGD1 were enrolled in this study.

Pre-assignment

Screening details:

Participants who met all inclusion criteria and none of the exclusion criteria were enrolled in 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	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Avacincaptad Pegol

Arm description:

The participants received ACP 2 mg/eye on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: ACP 2 mg/eye
o D14: ACP 2 mg/eye
And the participants then received ACP 4 mg/eye monthly (Month 3 – Month 17) in the Maintenance Phase.

Arm type	Experimental
Investigational medicinal product name	avacincaptad pegol
Investigational medicinal product code	ARC1905
Other name	Zimura (previous name) Izervay
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Intravitreal Injection

Arm title	Sham

Arm description:

The participants received Sham on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: Sham
o D14: Sham
And the participants then received Sham monthly (Month 3 – Month 17) in the Maintenance Phase.

Arm type	Placebo
Investigational medicinal product name	sham
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Intravitreal Injection

Number of subjects in period 1	Avacincaptad Pegol	Sham
Started	61	60
Safety Analysis Set (SAF)	61	58
Completed	44	53
Not completed	17	7
Adverse event, serious fatal	1	-
Adverse event, non-fatal	4	1
Other	2	1
Subject request	7	3
Lost to follow-up	2	-
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Avacincaptad Pegol
Reporting group description:	
The participants received ACP 2 mg/eye on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase: o D0: ACP 2 mg/eye o D14: ACP 2 mg/eye And the participants then received ACP 4 mg/eye monthly (Month 3 – Month 17) in the Maintenance Phase.	
Reporting group title	Sham
Reporting group description:	
The participants received Sham on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase: o D0: Sham o D14: Sham And the participants then received Sham monthly (Month 3 – Month 17) in the Maintenance Phase.	

Reporting group values	Avacincaptad Pegol	Sham	Total
Number of subjects	61	60	121
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)	61	60	121
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	33.8	36.1	
standard deviation	± 7.90	± 10.58	-
Gender, Male/Female Units: Participants			
Female	41	31	72
Male	20	29	49
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	1	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	6	9
White	55	53	108
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12	14	26
Not Hispanic or Latino	49	46	95
Unknown or Not Reported	0	0	0
Area of Ellipsoid Zone Defect			
The area of ellipsoid zone defect was measured by en face spectral domain-optical coherence tomography. ITT included all participants who were randomized. Participants were analyzed according to the treatment to which they were assigned at the time of randomization regardless of the actual study drug the participant may have received during the participation in the study. Only participants with available data at Baseline were included.			
Units: mm^2			
arithmetic mean	4.31	3.94	
standard deviation	± 4.85	± 2.46	-

End points

End points reporting groups

Reporting group title	Avacincaptad Pegol

Reporting group description:

The participants received ACP 2 mg/eye on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: ACP 2 mg/eye
o D14: ACP 2 mg/eye
And the participants then received ACP 4 mg/eye monthly (Month 3 – Month 17) in the Maintenance Phase.

Reporting group title	Sham

Reporting group description:

The participants received Sham on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: Sham
o D14: Sham
And the participants then received Sham monthly (Month 3 – Month 17) in the Maintenance Phase.

Primary: Mean Rate of Change in the Area of Ellipsoid Zone Defect from Baseline through Month 18

End point title	Mean Rate of Change in the Area of Ellipsoid Zone Defect from Baseline through Month 18

End point description:

The area of ellipsoid zone defect was measured by en face spectral domain-optical coherence tomography. Rate of change (slope) in the area of ellipsoid zone defect from Baseline through Month 18 was estimated using mixed model for repeated measures (MMRM).

ITT included all participants who were randomized. Participants were analyzed according to the treatment to which they were assigned at the time of randomization regardless of the actual study drug the participant may have received during the participation in the study. Participants with either a non-missing baseline or non-missing post-baseline assessment were included.

End point type	Primary

End point timeframe:

Baseline to Month 18

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	58		
Units: mm^2/18 months				
least squares mean (standard error)	0.6383 (± 0.1113)	0.6644 (± 0.1081)		

Statistical analyses

Statistical analysis title	ACP versus (vs.) Sham
Comparison groups	Avacincaptad Pegol v Sham

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8669
Method	Mixed models analysis
Parameter estimate	difference in LS mean
Point estimate	-0.0261
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3334
upper limit	0.2813
Variability estimate	Standard error of the mean
Dispersion value	0.1551

Secondary: Change in Best Corrected Visual Acuity (BCVA) Using Early Treatment Diabetic Retinopathy Study (ETDRS) Letters from Baseline at Month 18

End point title	Change in Best Corrected Visual Acuity (BCVA) Using Early Treatment Diabetic Retinopathy Study (ETDRS) Letters from Baseline at Month 18

End point description:

BCVA in the study eye was assessed using ETDRS visual acuity testing chart. The ETDRS Visual Acuity Score (ETDRS letters) is calculated based on the number of letters read on the ETDRS chart. Minimum and maximum possible scores are 0-100. A higher score represented increased visual functioning. A positive change from Baseline indicates an decrease in symptomology. Change in BCVA from Baseline at Month 18 was estimated using MMRM.

ITT included all participants who were randomized. Participants were analyzed according to the treatment to which they were assigned at the time of randomization regardless of the actual study drug the participant may have received during the participation in the study. Participants with a non-missing baseline and at least one non-missing post-baseline assessment were included.

End point type	Secondary

End point timeframe:

Baseline and Month 18

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	58		
Units: ETDRS letters				
least squares mean (standard error)	-0.1326 (± 1.2080)	-1.3358 (± 1.1622)		

Statistical analyses

Statistical analysis title	ACP vs. Sham
Comparison groups	Avacincaptad Pegol v Sham

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4745
Method	Mixed models analysis
Parameter estimate	difference in LS mean
Point estimate	1.2032
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1196
upper limit	4.5259
Variability estimate	Standard error of the mean
Dispersion value	1.6765

Secondary: Change in Photopic or Mesopic Macular Sensitivity Measured by Microperimetry from Baseline at Month 18

End point title	Change in Photopic or Mesopic Macular Sensitivity Measured by Microperimetry from Baseline at Month 18

End point description:

Photopic macular sensitivity or mesopic macular sensitivity were measured by microperimetry. Participants either had a photopic or mesopic measurement taken depending on the resources available at their site. Researchers were provided with one measurement regardless of the type of lighting conditions the assessment was conducted in. A higher score represented an increased retinal sensitivity. A positive change from Baseline indicates an improvement in symptomology. Change in Photopic or Mesopic Macular Sensitivity from Baseline at Month 18 was estimated using MMRM.

ITT included all participants who were randomized. Participants were analyzed according to the treatment to which they were assigned at the time of randomization regardless of the actual study drug the participant may have received during the participation in the study. Participants with a non-missing baseline and at least one non-missing post-baseline assessment were included.

End point type	Secondary

End point timeframe:

Baseline and Month 18

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: dB				
least squares mean (standard error)	-1.1604 (± 0.7964)	-1.9184 (± 0.8128)		

Statistical analyses

Statistical analysis title	ACP vs. Sham
Comparison groups	Avacincaptad Pegol v Sham

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5145
Method	Mixed models analysis
Parameter estimate	difference in LS mean
Point estimate	0.758
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.592
upper limit	3.108
Variability estimate	Standard error of the mean
Dispersion value	1.1487

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

An AE is defined as any untoward medical occurrence in a participant including unfavorable and unintended signs, symptoms or disease temporally associated with the use of a medicinal product and which does not necessarily have to have a causal relationship to this treatment.
AEs include illnesses with onset during the trial, or exacerbations of pre-existing illnesses. Exacerbation of pre-existing illness is defined as a significant increase in the severity of the illness as compared to the start of the trial and was considered when a participant requires new or additional treatment for that illness. Lack of or insufficient clinical response or efficacy was not recorded as an AE.

Safety Analysis Set (SAF) included all participants who received at least one dose of study drug. Participants were analyzed in the ACP group if they ever received ACP at any time during the study. Participants that received Sham and never received ACP were analyzed in the Sham group.

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	58		
Units: Participants	53	45		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose up to 18 months

Adverse event reporting additional description:

SAF included all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v24.1

Reporting groups

Reporting group title	Sham

Reporting group description:

The participants received Sham on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: Sham
o D14: Sham
And the participants then received Sham monthly (Month 3 – Month 17) in the Maintenance Phase.

Reporting group title	Avacincaptad Pegol

Reporting group description:

The participants received ACP 2 mg/eye on Day 1, Month 1, and Month 2 in the following sequence, 14 days apart in the Induction Phase:
o D0: ACP 2 mg/eye
o D14: ACP 2 mg/eye
And the participants then received ACP 4 mg/eye monthly (Month 3 – Month 17) in the Maintenance Phase.

Serious adverse events	Sham	Avacincaptad Pegol	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 58 (3.45%)	3 / 61 (4.92%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Eye disorders			

Endophthalmitis			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotony of eye			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sham	Avacincaptad Pegol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 58 (70.69%)	47 / 61 (77.05%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 58 (0.00%)	10 / 61 (16.39%)	
occurrences (all)	0	58	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 58 (6.90%)	2 / 61 (3.28%)	
occurrences (all)	4	2	
Ligament sprain			
subjects affected / exposed	4 / 58 (6.90%)	1 / 61 (1.64%)	
occurrences (all)	4	1	
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	
occurrences (all)	3	1	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 58 (15.52%)	9 / 61 (14.75%)	
occurrences (all)	30	30	
Eye disorders			
Dry eye			
subjects affected / exposed	5 / 58 (8.62%)	4 / 61 (6.56%)	
occurrences (all)	5	4	
Conjunctival oedema			
subjects affected / exposed	0 / 58 (0.00%)	5 / 61 (8.20%)	
occurrences (all)	0	26	
Eye pain			
subjects affected / exposed	7 / 58 (12.07%)	9 / 61 (14.75%)	
occurrences (all)	10	24	
Ocular hyperaemia			
subjects affected / exposed	1 / 58 (1.72%)	4 / 61 (6.56%)	
occurrences (all)	1	6	
Punctate keratitis			
subjects affected / exposed	4 / 58 (6.90%)	8 / 61 (13.11%)	
occurrences (all)	6	13	
Seasonal allergy			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	
occurrences (all)	4	1	
Vision blurred			
subjects affected / exposed	3 / 58 (5.17%)	4 / 61 (6.56%)	
occurrences (all)	3	4	
Vitreous detachment			
subjects affected / exposed	1 / 58 (1.72%)	4 / 61 (6.56%)	
occurrences (all)	1	4	
Vitreous floaters			
subjects affected / exposed	1 / 58 (1.72%)	7 / 61 (11.48%)	
occurrences (all)	1	9	
Conjunctival haemorrhage			

subjects affected / exposed	10 / 58 (17.24%)	31 / 61 (50.82%)	
occurrences (all)	21	140	
Conjunctival hyperaemia			
subjects affected / exposed	5 / 58 (8.62%)	6 / 61 (9.84%)	
occurrences (all)	13	9	
Eye irritation			
subjects affected / exposed	5 / 58 (8.62%)	8 / 61 (13.11%)	
occurrences (all)	15	12	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 58 (0.00%)	5 / 61 (8.20%)	
occurrences (all)	0	6	
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	
occurrences (all)	3	1	
Influenza			
subjects affected / exposed	5 / 58 (8.62%)	0 / 61 (0.00%)	
occurrences (all)	5	0	
Nasopharyngitis			
subjects affected / exposed	11 / 58 (18.97%)	12 / 61 (19.67%)	
occurrences (all)	19	13	
Sinusitis			
subjects affected / exposed	3 / 58 (5.17%)	3 / 61 (4.92%)	
occurrences (all)	3	3	
Urinary tract infection			
subjects affected / exposed	4 / 58 (6.90%)	6 / 61 (9.84%)	
occurrences (all)	4	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported