



## Clinical trial results:

**An open label, multi-centre, Phase I/II dose escalation trial of a recombinant adeno-associated virus vector (AAV2/8-hCARp.hCNGB3) for gene therapy of adults and children with achromatopsia owing to defects in CNGB3**

### Summary

EudraCT number	2016-002290-35
Trial protocol	GB
Global end of trial date	25 October 2019

### Results information

Result version number	v1 (current)
This version publication date	26 August 2021
First version publication date	26 August 2021

### Trial information

#### Trial identification

Sponsor protocol code	MGT006
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	MeiraGTx II UK Ltd
Sponsor organisation address	34-38 Provost Street, London, United Kingdom, N17NH
Public contact	Julie Bakobaki, MeiraGTx II UK Ltd, +44 2038664320, julie.bakobaki@meiragtx.com
Scientific contact	Julie Bakobaki, MeiraGTx II UK Ltd, +44 2038664320, julie.bakobaki@meiragtx.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	20 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2019
Global end of trial reached?	Yes
Global end of trial date	25 October 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to assess the safety of an AAV8 vector for hCNGB3 gene replacement in the retina.

Protection of trial subjects:

Only participants who met the study entry criteria were enrolled in the study. All participants were free to withdraw from the study at any time for any reason. All participants were closely monitored throughout the study. In addition, safety was evaluated based on adverse events (including dose-limiting events), clinical laboratory assessments, vital sign measurements, and physical examinations.

Background therapy:

None

Evidence for comparator:

n/a

Actual start date of recruitment	16 January 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	23
EEA total number of subjects	0

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)	6

Adolescents (12-17 years)	7
Adults (18-64 years)	10
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

n/a

### Period 1

Period 1 title	Dose-escalation phase/ Expansion Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

n/a

### Arms

<b>Arm title</b>	AAV8-hCARp.hCNGB3 gene therapy
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Arm description:

Study participants were administered a single dose in the worse-seeing eye at one of four dose levels.

Arm type	Experimental
Investigational medicinal product name	AAV8-hCARp.hCNGB3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subretinal use

Dosage and administration details:

subjects were administered a single subretinal dose

<b>Number of subjects in period 1</b>	AAV8-hCARp.hCNGB3 gene therapy
Started	23
Completed	23

## Baseline characteristics

### Reporting groups

Reporting group title	Dose-escalation phase/ Expansion Phase
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Reporting group description: -

Reporting group values	Dose-escalation phase/ Expansion Phase	Total	
Number of subjects	23	23	
Age categorical			
median			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	6	6	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	10	10	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Age			
Units: years			
median	13.0		
full range (min-max)	5 to 33	-	
Gender categorical			
Units: Subjects			
Female	18	18	
Male	5	5	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	23	23	

### Subject analysis sets

Subject analysis set title	Safety Analysis Set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Safety Analysis Set (all enrolled participants who were administered ATIMP)

<b>Reporting group values</b>	Safety Analysis Set		
Number of subjects	23		
Age categorical			
median			
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)	6		
Adolescents (12-17 years)	7		
Adults (18-64 years)	10		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Age			
Units: years			
median	13.0		
full range (min-max)	5 to 33		
Gender categorical			
Units: Subjects			
Female	18		
Male	5		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	23		

## End points

### End points reporting groups

Reporting group title	AAV8-hCARp.hCNGB3 gene therapy
Reporting group description:	Study participants were administered a single dose in the worse-seeing eye at one of four dose levels.
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	Safety Analysis Set (all enrolled participants who were administered ATIMP)

### Primary: Primary Safety outcomes

End point title	Primary Safety outcomes <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	Occurring during the 6 weeks following ATIMP administration

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a single group study.

End point values	AAV8-hCARp.hCNGB3 gene therapy	Safety Analysis Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23	23		
Units: Number of events	23	23		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

To last visit (Week 24 after ATIMP administration)

Adverse event reporting additional description:

Most ocular AEs were temporally related to surgery, mild in severity and resolved with little or no intervention. For example, transient reduction in visual acuity was related to manipulation of the eye during surgery and all such AEs resolved within 38 days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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### Reporting groups

Reporting group title	Safety Analysis Set
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Reporting group description:

all enrolled participants who were administered ATIMP

<b>Serious adverse events</b>	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 23 (8.70%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Uveitis			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Safety Analysis Set		
Total subjects affected by non-serious adverse events subjects affected / exposed	23 / 23 (100.00%)		
Investigations Intraocular pressure increased subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 6		
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Visual field defect subjects affected / exposed occurrences (all)  Dizziness subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 6  5 / 23 (21.74%) 5  4 / 23 (17.39%) 4		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 3		
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)  Lenticular opacities subjects affected / exposed occurrences (all)  Visual acuity reduced subjects affected / exposed occurrences (all)  Subretinal fluid subjects affected / exposed occurrences (all)  foreign body sensation in eye subjects affected / exposed occurrences (all)	20 / 23 (86.96%) 20  15 / 23 (65.22%) 15  15 / 23 (65.22%) 15  9 / 23 (39.13%) 9  8 / 23 (34.78%) 8		

Ocular discomfort			
subjects affected / exposed	8 / 23 (34.78%)		
occurrences (all)	8		
Chorioretinal folds			
subjects affected / exposed	6 / 23 (26.09%)		
occurrences (all)	6		
Retinal haemorrhage			
subjects affected / exposed	6 / 23 (26.09%)		
occurrences (all)	6		
Conjunctival hyperaemia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Eye inflammation			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Maculopathy			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Retinal depigmentation			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Retinal oedema			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Retinal tear			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
eye pain			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Photophobia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Vitreous floaters			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		

Conjunctival oedema subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Corneal disorder subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Macular fibrosis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Retinal disorder subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Retinal pigment epitheliopathy subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Uveitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	8 / 23 (34.78%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Infections and infestations Postoperative wound infection subjects affected / exposed occurrences (all)  Rhinitis	2 / 23 (8.70%) 2		

subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	5		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2017	Protocol v1.0 to v2.0 - Clarifications to outcome assessments, definitions and risks
08 March 2018	Protocol v2.0 to v3.0 - Clarifications in risks and trial design for expansion phase, addition of sample
15 May 2018	Protocol v3.0 to V4.0 - Updates to risks, clarifications in outcome assessments & surgical procedure.
19 December 2018	Protocol V4.0 to v5.0 - Increase in sample size, clarifications in dosing 19-Dec-2018 - Protocol v5.0 to v6.0 - HRA requested clarification on dosing (This led SA04 to be withdrawn and subsequent submission of SA05)
07 February 2019	Protocol v6.0 to v7.0 - Updates to secondary outcome assessments

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported