Phase 3 Follow-up Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene

Published: 18-10-2021
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This study has been transitioned to CTIS with ID 2024-511411-25-00 check the CTIS register for the current data. Main objective:To assess the long-term safety and tolerability of AAV5-hRKp.RPGR in individuals with RPGR-XLRPTo assess the long-term...

Ethical review	Approved WMO
Status	Pending
Health condition type	Congenital eye disorders (excl glaucoma)
Study type	Interventional

Summary

ID

NL-OMON51971

Source
ToetsingOnline

Brief title
MGT-RPGR-022 Gene therapy follow-up study in patients with XLRP

Condition

- Congenital eye disorders (excl glaucoma)

Synonym
genetic eye disease, XLRP

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag International NV

Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: AAV5-hRKp.RPGR, Follow-up, Phase III, XLRP

Outcome measures

Primary outcome

Efficacy: Change from baseline in binocular vision-guided mobility assessment (VMA) after bilateral subretinal delivery of AAV5-hRKp.RPGR

Adverse Events

Laboratory Assessment

Secondary outcome

Major secondary efficacy endpoints will include the following:

•Retinal Function assessed by

- Change from baseline in mean retinal sensitivity within the central 10 degrees excluding scotoma (MRS10) in static perimetry

- Change from baseline in mean retinal sensitivity of worse-seeing eye within the central 10 degrees excluding scotoma (MRS10) in static perimetry

- Pointwise response in full visual field

- Pointwise response in worse-seeing eye in full visual field

- Pointwise response in the central 30 degrees visual field

- Pointwise response in worse-seeing eye in the central 30 degrees visual field

- Change from baseline in mean retinal sensitivity within the full visual

field excluding scotoma (MRS90) in static perimetry

•Functional Vision assessed by

- Vision-guided mobility assessment response in the "worse-seeing eye"

as assessed by VMA

- Change from baseline in the modified Low Luminance Questionnaire

(mLLQ) - Extreme lighting domain score

•Visual Function assessed by

- Change from baseline in low luminance visual acuity by Early

Treatment Diabetic Retinopathy Study (ETDRS) chart letter score in

monocular assessment

- Change from baseline in best corrected visual acuity (BCVA) by ETDRS

chart letter score in monocular assessment

- Change from baseline in low luminance visual acuity by ETDRS chart

letter score in worse-seeing eye

Study description

Background summary

Retinitis pigmentosa (RP) constitutes a group of inherited diseases of the retina characterized by a progressive reduction in vision, initially manifest as nyctalopia (night blindness) that usually becomes apparent in childhood or early adulthood and is progressive throughout the individual*s lifetime (Tee 2016).

No therapies are approved for any form of RP, and the condition is serious and progressive. There is a real possibility that gene therapy could offer a significant benefit in terms of markedly slowing or halting progressive retinal loss thereby preserving central vision and improving sight and quality of life (QoL). The approval of Voretigene Neparvovec (Luxturna, Spark Therapeutics) for biallelic RPE65 disease (Russell 2017) provides convincing proof of concept. This is reinforced by our own experience from the first gene therapy study for inherited retinal disease (Bainbridge 2008) and pre-clinical data demonstrating improved outcome in animal models of RPGR-XLRP. Preliminary data from the ongoing Study MGT009 has also demonstrated significant improvement in both visual function (as determined by assessment of visual fields by static perimetry), and functional vision (as determined by a visual mobility assessment in low illumination levels) (see Section 2.2, Background).

Taking into account the measures taken to minimize risk to participants of this study and the preliminary efficacy results of the MGT009 study, the potential risks identified in association with AAV5-hRKp.RPGR are justified by the anticipated benefits that may be afforded to participants with RPGR-XLRP

Study objective

This study has been transitioned to CTIS with ID 2024-511411-25-00 check the CTIS register for the current data.

Main objective:

To assess the long-term safety and tolerability of AAV5-hRKp.RPGR in individuals with RPGR-XLRP
To assess the long-term efficacy of treatment with AAV5-hRKp.RPGR in individuals with RPGR-XLRP based on assessments of functional vision as measured by vision-guided mobility assessment (VMA).

Secondary objectives:
To assess changes in all participants after treatment in: retinal function,functional vision, visual function

Study design

This is a long-term, safety follow-up study of participants who participated in Study MGT-RPGR-021; the study also allows for initial treatment of participants who were randomly assigned to deferred treatment in MGT-RPGR-021. Participants will be male and female, aged 3 years and older who participated in and completed Study MGT-RPGR-021. For participants who are eligible for treatment in this study, AAV5-hRKp.RPGR gene therapy will be administered by

subretinal injection using a standardized surgical procedure; all participants will be offered bilateral treatment, with the second eye treated 7 to 21 days after the first.

An Independent Data Monitoring Committee (IDMC) will be commissioned for this study to
provide expert input on safety of the investigational product, surgical procedure, and related issues.

Follow-up period: All study participants must be followed for a period of 60 months after the treatment:
Participants who were randomly assigned to immediate treatment in Study MGT-RPGR-021 will transition directly to a long-term follow-up schedule, beginning with a study visit at Month 18 posttreatment, to complete an additional 48 months of follow-up.

- Participants who were randomly assigned to deferred treatment in Study MGT-RPGR-021 will transition to a treatment schedule, including a review of eligibility criteria and new baseline evaluations within 2 months after completion of Study MGT-RPGR-021, followed by bilateral treatment. Upon completion of the 52-week primary treatment period, this cohort will enter the long-term follow-up schedule, to complete a total of 60 months follow-up.

Intervention

AAV5-hRKp.RPGR gene therapy is injected in the subretinal space of the treatment eye in the operating room by a retinal surgeon who is trained and qualified to deliver the investigational product. Delivery of vector liquid to the subretinal space will be performed following standard surgical vitrectomy. This will involve a 3-port pars plana vitrectomy followed by injection of vector liquid using a fine cannula through
a small retinotomy into the subretinal space, resulting in a transient retinal detachment. One or more retinotomies may be used. A pre-bleb (with, eg, balanced salt solution) is not allowed.

Eligible participants who were assigned to deferred treatment in Study MGT-RPGR-021 will be treated bilaterally with either RPGR2e11 dose (in up to 800 µL in each eye) or RPGR4e11 dose (in up to 800 µL in each eye). The total volume of injection should not exceed 0.8 mL. Previous gene therapy clinical studies have shown that the bleb of subretinal vector liquid is expected to resolve spontaneously over the course of the first 24 to 48 hours postoperatively as the fluid is resorbed by the underlying retinal pigment epithelium.

All treatment-eligible participants will receive bilateral treatment, with surgical delivery to the 2 eyes performed within 7 to 21 days apart. The first eye treated will be the worst-seeing eye as determined by visual acuity and

static perimetry, and the second eye will receive identical treatment. In the event of a significant ocular adverse event in the first eye or any other intercurrent issue that persists through Day
21, the investigator will consult with the sponsor*s Medical Monitor about the risks, benefits, and timing of treatment to the second eye.
If both visual acuity and MRS are equal in both eyes, the right eye will be the first eye
receiving treatment.

To minimize the occurrence and severity of immune response to the investigational product, all participants will receive a defined regimen of systemic immune suppression initiated prior to and continued following the completion of surgery.

Study burden and risks

For full details, see Table 1.3 in the Protocol Table 1 and Table 2 on page 14-18

Patient participation in this study lasts approximately 4 years for group 1 and 5 years for group 2. During this time, the patient in group 1 (immediate treatment) will visit the hospital approximately 5 times and 15 times in group 2 (delayed treatment until study022). The visits last approximately 2-9 hours.
The following tests and procedures are performed during these visits:
- Physical exam, vital signs, demographic and medical history
- Questionnaires
- Blood and urine tests
- Pregnancy tests in women of childbearing potential
- tears sample and saliva samples
- various eye tests and images of the eye
- visual mobility assessments
- patients participate in interviews
- Patients in Group 2 will receive the study drug via retinal injection via surgical vitrectomy. The second eye is treated 7-21 days after the first eye
- Female patients: breastfeeding is not allowed. Effective contraceptive methods should be used during the study and for 6 months after the last dose of the study drug from the time of signing the ICF.
- Male patients: Due to the potential risk of the effect on sperm, an appropriate method of contraception should be used from
screening and during the study and for at least 6 months after the last dose of study drug
Possible side effects that are already known are described in the IB and patient information letter.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

1.Previously completed participation in Study MGT-RPGR-021.
2.Must reconfirm that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study.

Exclusion criteria

There are no specific exclusion criteria.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	28-02-2022
Enrollment:	3
Type:	Anticipated

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Botaretigene Sparoparvovec
Generic name:	AAV5-hRKp.RPGR

Ethics review

Approved WMO Date:	18-10-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-03-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	14-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-06-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-01-2024
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-02-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-04-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-06-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	04794101
EU-CTR	CTIS2024-511411-25-00
EudraCT	EUCTR2020-002255-37-NL
CCMO	NL75522.000.21