A Phase 3 Randomized, Masked, Controlled Trial to Evaluate Efficacy and Safety of Belzupacap Sarotalocan (AU-011) Treatment Compared to Sham Control in Subjects with Primary Indeterminate Lesions or Small Choroidal Melanoma

Published: 27-05-2024
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Primary: To determine the efficacy and safety of bel-sar compared to sham control for thetreatment of primary indeterminate lesions and small choroidal melanoma (IL/CM).Secondary: To assess the systemic pharmacokinetics (PK) and immunogenicity of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Interventional

Summary

ID

NL-OMON56772

Source
ToetsingOnline

Brief title
AU-011-301-MD1

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders
- Ocular neoplasms

Synonym

Eye cancer

Research involving
Human

Sponsors and support

Primary sponsor: Aura Biosciences, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: bel-sar (AU-011), Phase 3, Primary Indeterminate Lesions, Small Choroidal Melanoma

Outcome measures

Primary outcome

Primary: (80 µg treatment arm)

Time to reach Tumor Progression (at the Week 65 analysis).

Secondary outcome

Key Secondary:

*Time to reach the Composite Endpoint 80 µg (at the Week 65 analysis).

*Time to reach Visual Acuity Failure 80 µg (at the Week 65 analysis).

*Time to reach Tumor Progression 80 µg (at the Week 104 analysis).

*Time to reach Visual Acuity Failure 80 µg (at the Week 104 analysis).

*Time to reach the Composite Endpoint 80 µg (at the Week 104 analysis).

*Time to reach Tumor Progression 40 µg (at the Week 65 analysis)

Study description

Background summary

Sponsor is currently developing an investigational treatment called belzupacap sarotalocan(bel-sar), which is administered into the eye using an

investigational device called a microinjector (made by a company called Clearside Biomedical Inc), after which the drug (bel-sar) is activated by investigational laser system (made by Quantel Medical or Modulight) for the treatment of choroidal melanoma (CM). Investigational means that this treatment has not been approved as a marketed product (ie, available to be prescribed or sold) by any regulatory authorities in The Netherlands.

Study objective

Primary: To determine the efficacy and safety of bel-sar compared to sham control for the
treatment of primary indeterminate lesions and small choroidal melanoma (IL/CM).

Secondary: To assess the systemic pharmacokinetics (PK) and immunogenicity of bel-sar
with suprachoroidal (SC) administration.

Study design

This is a randomized, sham-controlled, subject-, assessor-, and Sponsor-masked trial to establish
the efficacy and safety of bel-sar treatment via SC administration in subjects with primary IL/CM.
Bel-sar treatment incorporates administration of bel-sar drug product using the SCS Microinjector
and activation of bel-sar by a laser photoactivation device (Quantel Vitra Aura Laser modified for
specific use with bel-sar). The trial will employ an enrichment strategy with enrollment of subjects
with early documented growth of IL/CM. This will ensure that subjects have actively growing
lesions allowing for a reduction in the variability of timing and event rates of selected endpoints
being used to establish the efficacy of bel-sar treatment. The trial will be conducted at sites that
evaluate and document tumor growth as part of their practice prior to treating IL/CM. Subjects
with clinically diagnosed IL/CM, that have recent documented tumor growth for whom
observation-only (i.e., a watchful waiting approach) could be an appropriate SoC per Investigator's
judgment, will qualify for this trial

Intervention

Once eligibility is confirmed, qualified subjects will be randomly assigned to

1 of 3 treatment arms
(80 µg bel-sar treatment arm, 40 µg bel-sar treatment arm, or sham control arm).

The bel-sar treatment arms will receive 3 cycles of treatment at the assigned dose and the sham
control arm will receive 3 cycles of sham treatment. One cycle is defined as once/week treatment
(bel-sar and laser for the 2 bel-sar treatment arms or sham injection and sham laser for the sham
control arm) administered for 3 consecutive weeks (e.g., Cycle 1 treatments will occur on Days 1,
8, and 15). Cycle 2 is planned to initiate at Week 4 and Cycle 3 at Week 8.

Study burden and risks

Microinjector
According to the manufacturer of this microinjector, in controlled studies, the most common ocular adverse reactions were increased intraocular pressure (IOP), acute (6%), vitreous detachment (5%), injection site pain (4%) conjunctival haemorrhage (4%), visual acuity reduced (4%), dry eye (3%), eye pain, acute (3%), photophobia (3%), and vitreous floaters (3%), and in 2% of patients: conjunctival hyperaemia, punctate keratitis, conjunctival oedema, meibomianitis, anterior capsule contraction, chalazion, eye irritation, eye pruritus, eyelid ptosis, photopsia, and vision blurred. The most common non-ocular AE was headache (5%).

Laser
Although they are rare, the laser treatment carries a few potential risks. These include temporary vision changes such as blurred or decreased vision, increased light sensitivity for a few days or weeks, and possible eye discomfort or pain during or after the procedure.
While infection or inflammation are uncommon, they can occur at the treatment site, necessitating further medical attention. Additionally, although extremely rare, there is a slight risk of retinal detachment, indicated by symptoms like increased floaters or flashes of light.

You may have side effects from the laser light application (or sham procedure). You will be carefully monitored for any side effects. However, researchers do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop receiving the laser or sham procedure. In some cases, side effects can be serious, long lasting, or may never go away. Call the investigator right away if you have, or believe you may have, any side effects.

In an ongoing second study of bel-sar in which bel-sar was given by

suprachoroidal injection, 20 participants with eye melanoma have been enrolled as of 03 February 2023. The most common side effects of laser treatment were inflammation in the front of the eye, eye redness, eye pain, or irritation on the cornea.

Contacts

Public
Aura Biosciences, Inc.

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Ocular inclusion criteria apply to the study eye only unless specifically stated otherwise.
Subject must:
1. Be at least 18 years of age.
2. Have been informed about the nature and requirements of the trial, voluntarily agreed

to participate in the trial and follow all trial procedures and documented their consent
by signing the Informed Consent Form before participating in any trial-related activities.
3. Have no evidence of metastatic disease confirmed per the SoC and at a minimum by
abdominal and chest imaging within 2 months prior to enrollment.
4. Be treatment naïve for their IL/CM (Note: eligibility for subjects who have received
treatment with photodynamic therapy >12 months prior to enrollment should be discussed with the medical monitor for approval prior to enrollment).
5. Have per the Investigator*s expert clinical judgment, a clinical diagnosis of primary
IL/CM based on the clinical history, ophthalmic examination, FP and conventional ocular ultrasound for whom observation-only (i.e., a watchful waiting approach) would
be a recommended standard of care.

Exclusion criteria

1. Have in the Investigator's opinion, any active ocular infection or ocular disease in the study
eye (other than IL/CM) that may progress during the trial and result in a change in vision,
loss in vision, confound the trial assessments, or alter the SCS (e.g., clinically significant
corneal dystrophies, keratoconus, glaucoma or clinically significant choroidal, retinal,
macular, or scleral disease). Subjects who have a known history of steroid induced glaucoma
or high myopia (>=-6.00 diopters) are also excluded.
2. Have an IL/CM that is in contact with the optic disc >=6 clock hours/>=180 degrees
(based on true-color FP) per IRC or an IL/CM that invades the optic nerve per the
Investigator's judgement.
3. Have evidence of extraocular extension or evidence of a break in Bruch's membrane
(i.e., the tumor has spread outside the choroid) per the Investigator's judgment.
4. Have undergone any ocular surgical intervention in the study eye within 3 months before
Visit 1 or are planning/will require ocular surgery in the study eye during the trial.
Subjects who have had an uncomplicated minor procedure or cataract surgery

within 1-
3 months of Visit 1 should be discussed on a case-by-case basis with the medical monitor
for approval prior to enrollment. Laser surgery (e.g., refractive laser surgery, argon laser
trabeculoplasty/selective laser trabeculoplasty [ALT/SLT], and other minimally invasive
surgeries [e.g., minimally invasive glaucoma surgery {MIGS}]) within 3 months of Visit
1 should be discussed with the medical monitor for approval prior to enrollment.
5. Have a history of any ocular surgery/procedure that could alter the SCS and affect SC
administration of bel-sar (e.g., scleral buckle, laser retinopexy, macular laser, or pan-
retinal photocoagulation).
6. Have an ETDRS-BCVA score worse than 65 letters in the study eye.
7. Use or require use of heparin or low molecular weight heparins within 1 week of any
trial treatment or pentosan polysulfate within a year prior to Visit 1.
8. Use or requires use of immunosuppressive or antineoplastic medications within 5
half-lives of Visit 1. Steroids, including inhalation steroids, are permitted.
Any active malignancies other than IL/CM, or squamous or basal cell skin cancer. If there
is evidence of clinical remission for at least 1 year, the subject's eligibility should be
discussed with the medical monitor for approval prior to enrollment.
9. Have any significant illness (e.g., an uncontrolled autoimmune disease, liver disease,
severe cardiovascular disease [confirmed by a cardiologist], active infection, etc.) or
clinically significant laboratory abnormalities that the Investigator determines could
interfere with trial participation or put the subject at any unnecessary risk.
10. Have used an investigational drug or medical device within 30 days or 5 half-lives
(whichever is longer) of Visit 1 or be concurrently enrolled in another IP trial.
11. Have known contraindications or sensitivities to phthalocyanine-based dye, the capsid
component, or to prior treatment with laser.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2024
Enrollment:	3
Type:	Anticipated

Medical products/devices used

Generic name:	The suprachoroidal space (SCS) Microinjector
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	27-05-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-09-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL85790.000.23