A Phase I/IIa Dose Escalation Safety Study of Subretinally Injected SAR422459, Administered to Patients with Stargardt's Macular Degeneration.

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The objectives of the study are to assess the safety and tolerability of ascending doses of SAR422459 in patients with Stargardt macular disease and to evaluate the possible biological activity of SAR422459.

Ethical review	Not approved
Status	Will not start
Health condition type	Eye disorders congenital
Study type	Interventional

Summary

ID

NL-OMON43680

Source
ToetsingOnline

Brief title
TDU13583

Condition

- Eye disorders congenital
- Vision disorders

Synonym
Fundus flavimaculatus, Stargardt disease

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Sanofi-aventis

Intervention

Keyword: Congenital disease, Gene therapy, Orphan, Stargardt disease

Outcome measures

Primary outcome

The primary endpoint will be considered at Week 48 and will evaluate:

- The incidence and severity of treatment emergent adverse events

- The clinically important changes from the baseline (best-corrected visual acuity (BCVA), intraocular pressure, slit lamp examination, fundoscopy/indirect ophtalmoloscopy, fundus photography, optical coherence tomography, microperimetry, full-field static and kinetic perimetry and ERG

Secondary outcome

To determine a delay in retinal degeneration following subretinal injection of SAR422459, through changes from baseline relative to the untreated contralateral eye on BCVA, microperimetry, full-field static and kinetic perimetry, OCT and fundus autofluorescence.

Study description

Background summary

Stargardt disease is the most prevalent inherited, orphan disease that causes visual impairment in children and young adults. In the absence of viable treatment options for this disease, gene therapy is considered as the most relevant/promising treatment approach. Following a successful and supportive non-clinical program, this First In Man study is aimed at investigating the

safety and potential biological activity of SAR422459 in Stargardt disease.

Study objective

The objectives of the study are to assess the safety and tolerability of ascending doses of SAR422459 in patients with Stargardt macular disease and to evaluate the possible biological activity of SAR422459.

Study design

Interventional open label study.

Intervention

Patients of cohort 6 (adults and children) will receive SAR422459 via a subretinal injection in the eye, after vitrectomy.

Study burden and risks

The total duration per patient is up to 52 weeks, which includes a 4 week screening period and a 48 weeks study period. There is a total of 10 visits with thorough eye examination, non-invasive ophthalmic investigations, Quality of Life questionnaire and blood sampling. The eye examination, ophthalmic investigations do not carry any risk but some can generate slight discomfort and require the patient attention and active participation.

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)
Elderly (65 years and older)

Inclusion criteria

Patients must meet ALL of the following criteria to be considered for enrolment into this study:;1. Signed and dated written informed consent obtained from the patient and/or the patient*s legally acceptable representative, if applicable, in accordance with the local regulations.;2. Diagnosis of SMD, with at least one pathogenic mutant ABCA4 allele on each chromosome, confirmed by direct sequencing.;3. Women of childbearing potential must have a negative pregnancy test at day -1 and agree to use an effective form of contraception for at least three months such as the contraceptive pill or intra uterine device, or be surgically sterile or postmenopausal, with the last menstrual period being over two years prior to enrolment (partners of study patients must agree to use barrier contraception for at least three months after SAR422459 administration).;4. Males must agree with their partner to use two forms of contraception, including one barrier method for at least three months following SAR422459 administration if their partner is of childbearing potential, or must be surgically sterile.;Specific Inclusion Criteria Patient Group D:;- Symptomatic patients (6 years and older) with childhood or young adult onset Stargardt's Macular Degeneration (eg, before age 26) with at least one pathogenic mutant ABCA4 allele on each chromosome confirmed by direct sequencing and co-segregation analysis within the patient*s family.;- Visual acuity of *20/200 in both eyes at the time of the screening visit.;- Patients are anticipated to experience rapid deterioration in visual function and/or retinal structure in the opinion of the study Investigator.

Exclusion criteria

1. Pre-existing eye conditions that would preclude the planned surgery or interfere with the interpretation of study endpoints: glaucoma or other primary optic neuropathy that has

resulted in significant visual field loss, corneal or significant lens opacities, active uveitis, retinopathy and maculopathy (other than that from Stargardt disease) that in the opinion of the investigator is causing significant visual loss, myopia greater than 8 diopters spherical equivalent.;2. Cataract surgery with intraocular lens implantation within 6 months of enrolment.;3. Aphakia or prior vitrectomy in the study eye.;4. Concomitant systemic diseases including those in which the disease itself, or the treatment for the disease, can alter ocular function. For instance malignancies whose treatment could affect central nervous system function, diabetes, juvenile rheumatoid arthritis or sickle cell disease.;5. Any intraocular surgery (other than study procedure) or laser in either eye planned within 6 months of Day 0.;6. Any contraindication to pupil dilation in either eye.;7. Any known allergy to any component of the delivery vehicle or diagnostic agents used during the study (e.g., fluorescein, dilation drops), or medications planned for use in the peri-operative period particularly topical, injected or systemic corticosteroids.;8. Any injectable intravitreal treatment to the treated eye or intravitreal device in the treated eye within 6 months prior to screening.;9. Any periocular injections of corticosteroids to the treated eye within 4 months prior to screening.;10. Laboratory test abnormalities or abnormalities in electrocardiogram, chest X-rays that in the opinion of the PI would make the patient unsuitable for participation in the study.;11. Significant intercurrent illness or infection during the 28 days prior to enrolment.;12. Pre-menopausal or non-surgically sterile women who are unwilling to use an effective form of contraception such as the contraceptive pill or intrauterine device.;13. Men or women who do not agree to use barrier contraception according to the inclusion criteria.;14. Alcohol or other substance abuse.;15. Contraindications to use of anesthesia (local or general, as appropriate).;16. Concurrent anti-retroviral therapy that would inactivate the investigational agent.;17. History of any investigational agent within 28 days prior to SAR422459 administration.;18. Participation in a prior ocular gene transfer therapy study.;19. Enrolment in any other clinical treatment study, for any condition, including those relating to SMD, throughout the duration of the SAR422459 TDU13583 study participation.;20. Current or anticipated treatment with anticoagulant therapy or the use of anticoagulation therapy within the four weeks prior to surgery.;21. A past medical history of HIV or hepatitis A, B or C infection.;22. Inability to comply with the demands of the study.;23. Women who are pregnant or are breastfeeding.;24. History or signs consistent with unilateral amblyopia (strabismic, anisometropic or stimulus deprivation).

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Not yet available
Generic name:	Not applicable

Ethics review

Approved WMO

Date:	02-02-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Not approved

Date:	24-02-2016
Application type:	First submission
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
EudraCT	EUCTR2010-023111-34-NL
ClinicalTrials.gov	NCT01367444
CCMO	NL52850.000.16