Open-label, randomized, two*arm, controlled study to assess the efficacy, safety, and tolerability of intravitreal (IVT) aflibercept compared to laser photocoagulation in patients with retinopathy of prematurity (ROP)

Published: 07-05-2019
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Interventional

Summary

ID

NL-OMON49302

Source
ToetsingOnline

Brief title
FIREFLEYE

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
retinopathy of prematurity, ROP

Research involving

Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer A.G.

Intervention

Keyword: Aflibercept, EYLEA, FIREFLEYE, ROP

Outcome measures

Primary outcome

- Proportion of patients with absence of active ROP and unfavorable structural outcomes at 24 weeks after starting study treatment.

Secondary outcome

- Number of requirement for intervention with a second treatment modality from baseline to week 24

- Recurrence of ROP from baseline to week 24

- To explore new ROP Activity Scale proposed by the International Neonatal Consortium from baseline to week 24

- Number of aflibercept administrations from baseline to week 24.

- Number of laser treatments from baseline to Week 24.

- Proportion of participants with ocular TEAEs and SAEs from baseline to week 24.

- Proportion of participants with systemic TEAEs and SAEs from baseline to week 24.

- Systemic exposure to free aflibercept (at expected maximum plasma concentration and during elimination period from plasma) determined by sparse

sampling from baseline to week 24.

- Presence of anti-drug antibodies before and 12 weeks after aflibercept

injection.

Study description

Background summary

Retinopathy of prematurity is a proliferative vascular retinopathy caused by an abnormal development of the vascularization of the peripheral retina in premature infants. It affects mainly newborns with a preterm gestational age (* 32 weeks) and very low birth weight (* 1500 g). ROP remains a major cause of childhood blindness globally. As ROP is characterized by incomplete vascularization of the retina in premature infants, it has also been associated with increased levels of VEGF. Upregulation of VEGF due to ischemia in the avascular retina may induce pathologic neovascularization and subsequently lead to retinal detachment and blindness, as seen in late stage ROP. Aflibercept inhibits these effects of VEGF. Based on the drug*s mode of action, aflibercept has a high potential to become an effective treatment option for the treatment of ROP.

Study objective

The purpose of this study is to confirm how well aflibercept works in babies with ROP, comparing it with laser therapy. The study also has the objective to demonstrate how safe aflibercept is when used in babies. We will also learn how the drug moves into, through and out of the body.

Study design

This is a phase 3, multicenter, randomized, 2-arm, open-label clinical study to assess the efficacy, safety, and tolerability of IVT aflibercept versus laser photocoagulation in subjects with ROP. The study consists of screening/baseline (1 or 2 visits), a 23-week treatment period (including retreatment and rescue treatment), and a final visit at Week 24 (up to Week 27 for subjects treated after Week 21).

Intervention

- Subjects randomized to aflibercept will receive a single intravitreal (IVT) injection of aflibercept 0.4 mg/0.01 mL per eligible eye at baseline.
- Subjects randomized to laser photocoagulation will undergo treatment in each

eligible eye at baseline. Laser ablation should be as complete as possible as judged by the investigator.

Study burden and risks

Treatment with lasertherapy and/or aflibercept may have some therapeutic benefit but this cannot be guaranteed. Please refer to section E9 for a detailed description of the risks associated with participation.

Participation in the study involves approximately 14 visits in a time period of 24 weeks with physical exams, bloodsampling and eye examinations as described in the protocol. Examinations including eye examinations and physical exams, will be performed at specific visits as described in the protocol and the patient information and informed consent forms.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1.Gestational age at birth * 32 weeks or birth weight * 1500 g, Type of Participant and Disease Characteristics, 2.Subjects with treatment-naïve ROP classified according to the International Classification for ROP in at least one eye as:, - Zone I Stage 1 plus, or 2 plus, or 3 non-plus or 3 plus, or Zone II Stage 2 plus or 3 plus, or AP-ROP, 3.Weight at baseline (day of treatment) * 800 g, 4.Male or female, 5.Signed informed consent from parent(s)/legally authorized representative(s) as described in Section 10.1.3 of the clinical trial protocol, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the clinical trial protocol

Exclusion criteria

Subjects are excluded from the study if any of the following *per subject* criteria are met. A potential study eye is excluded from the study if any of the *per eye* criteria are met:, Medical Conditions * per subject, 1.Known or suspected chromosomal abnormality, genetic disorder or syndrome, 2.Previous exposure to any IVT or systemic anti-VEGF agent, including maternal exposure during pregnancy and/or during breastfeeding, 3.Clinically significant neurological disease (eg, intraventricular hemorrhage grade 3 or higher, periventricular leukomalacia, congenital brain lesions significantly impairing optic nerve function, severe hydrocephalus with significantly increased intracranial pressure), 4.Pediatric conditions rendering the infant ineligible for study intervention at baseline or for repeated blood draws as evaluated by a NICU specialist and a study ophthalmologist, 5.Presence of active ocular infection within 5 days of the first treatment, Medical Conditions * per eye, 6.Advanced stages of ROP with partial or complete retinal detachment (ROP Stages 4 and 5), 7.ROP involving only Zone III , 8.Ocular abnormalities that may interfere with the administration of study intervention or assessment of the study primary endpoint , Prior/Concomitant Therapy * per subject, 9.Postnatal treatment with oral or intravenous corticosteroids at an equivalent dose of prednisone * 1 mg/kg/day for >2 weeks within 14 days of the first study intervention, Prior/Concomitant Therapy * per eye, 10.Previous surgical or nonsurgical treatment for ROP (IVT anti-VEGF injection, ablative laser therapy, cryotherapy, and vitrectomy) , Prior/Concurrent Clinical Study Experience, 11.Participation of the subject or the mother in other clinical trials requiring administration of investigational treatments (other than vitamins and minerals) at the time of screening, or within 30 days or 5 half-lives of administration of the previous study drug, whichever is longer.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-05-2020
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	EYLEA
Generic name:	aflibercept
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-05-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2019
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2018-002611-99-NL
CCMO	NL69813.056.19

Study results

Results posted: 17-01-2022

First publication
01-01-1900

URL result
Type
ext
Naam
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URL
Type
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Naam
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