ForPatients
by Roche

Diabetic Macular Edema

A Phase I, multicenter, open-label study of the safety, tolerability, pharmacokinetics, and immunogenicity of intravitreal injections of RO7446603 alone and co-administered with aflibercept in patients with diabetic macular edema

Trial Status	Trial Runs In	Trial Identifier
Recruiting	2 Countries	GR43828

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

Study of the safety, tolerability, processing by the body, and ability to provoke immune system response of ocular injections of RO7446603 alone and in combination with aflibercept in participants with diabetic macular edema

F. Hoffmann-La Roche Ltd (USA)	Phase 1
Sponsor	Phase

GR43828
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Both	Adult	No

Background and study aims

Diabetic macular edema (DME) is a serious eye condition that affects people with high blood sugar. DME results when the damaged blood vessels leak fluid and cause swelling, which blurs vision. If it worsens, the eye may begin to form new, abnormal blood vessels over the light-sensitive layers of nerve tissue at the back of the eye (retina), which can break easily and bleed, causing severe vision loss and even blindness. The development of a mode of treatment called anti-vascular endothelial growth factor (anti-VEGF) pharmacotherapy (medication) in the past 10 years has led to dramatic improvements in visual outcomes for patients with DME. RO7446603 may lead to stabilization of the diseased blood vessels and improve visual and structural (anatomical) outcomes in

DME compared with previous treatments. RO7446603 is an experimental drug. Health authorities have not yet approved RO7446603 for the treatment of DME or any other disease. The main aims of this study are to evaluate how safe RO7446603 is at different doses and to understand the way the body processes the drug, and to test RO7446603 when given with aflibercept (Eylea®), a standard approved treatment for patients with DME.

Who can participate?

People aged 18 years or more with DME

What does the study involve?

Participants will need to be a part of this study for about 6 months. The study will include the following periods:

1. A screening period of up to 28 days to check the eligibility of participants to take part in the study

2. A treatment period of up to 16 weeks for participants in groups 1 and 3 and 20 weeks for participants in group 2, where participants will receive single or multiple injections of RO7446603 in the eye, with or without aflibercept.

3. A follow-up period during which participants will have check-up visits with the study team either at the clinic or via telephone

The study will be conducted in three stages:

1. A single ascending dose stage, where participants will receive RO7446603 given as one single injection in the eye

2. A multiple-dose monotherapy stage, where participants will receive RO7446603, given as two injections in the eye 8 weeks apart

3. A multiple-dose co-administration stage, where participants receive RO7446603 given as two injections in the eye 8 weeks apart, along with four injections of aflibercept 4 weeks apart, in accordance with the approved drug label.

During this study, participants will have to visit the clinic 10-12 times, depending on the group to which they are assigned. Visits may last for 1-5 hours.

What are the possible benefits and risks of participating?

The participants' health may or may not improve in this study, but the information collected may help other people who have a similar medical condition in the future. Participants may have a side effect from the drugs (RO7446603 and aflibercept) or procedures used in this study. These can be mild to severe and even life-threatening, and they can vary from person to person.

Risks associated with RO7446603 include infection inside the eye, inflammation inside the eye, an immune or allergic response against the drug, and an increase or decrease in blood pressure.

Risks associated with aflibercept:

Important side effects: reduced vision, bloodshot eye (caused by bleeding of the membrane covering the white of the eye), eye pain, infection inside the eye, inflammation inside the eye, cloudiness of the lens of the eye (cataracts), detachment or tear of the retina (which may progress to cause a loss of vision), increase in fluid pressure inside the eye, blood clots blocking blood vessels, which may lead to stroke or heart attack, an immune response against the drug.

Very common side effects: a decrease in vision, bleeding in the back of the eye (retinal hemorrhage), bleeding on the surface of the front of the eye (conjunctival hemorrhage), eye pain.

Common side effects: separation of one of the layers in the back of the eye (retinal pigment epithelium detachment or tear), bleeding in the eye (vitreous hemorrhage), temporary increase in intraocular pressure (fluid pressure inside the eye), blurred vision, injection site pain, feeling that there is something in the eye (foreign body sensation in eyes), bleeding at the site of the injection, inflammation on the surface of the eye (punctate keratitis), degeneration of the back of the eye (retinal degeneration), clouding of the lens in the eye (cataract), damage to the front window of the eye (corneal erosion, corneal abrasion), small particles or spots in vision (vitreous floaters), separation of the vitreous humor from the back of the eye (vitreous detachment), increased tear production, swelling of the eyelids (eyelid edema), eye redness (conjunctival hyperemia)

Uncommon side effects: allergic reactions, inflammation of the internal parts of the eye (anterior chamber flare, uveitis, iritis, iridocyclitis), swelling and deposits in the front window of the eye (corneal edema), abnormal sensation in the eye, injection site irritation, infections inside the eye (endophthalmitis), retinal tear (formation of a small hole in the retina or detachment (separation of the retina from the back of the eye), clouding of the lens (lenticular opacities), damage to the front layer of the eye (corneal epithelium defect), eyelid irritation

Rare side effects: blindness, clouding of the lens in the eye due to trauma/injury (traumatic cataract), inflammation in the jelly-like filling of the eye (vitritis), collection of pus in the eye (hypopyon)

Participants may develop increased pressure within the eye when a medication is injected into the eye. Participants with a history of glaucoma may be at more risk with RO7446603. Participants receiving injections of medications into their eye have developed infections inside and/or outside the eye (endophthalmitis and/or periocular, and/or corneal infections), retinal detachment (separation of the retina from the underlying tissue), or cataracts (cloudiness of the eye lens). Some participants can also develop bleeding inside the eye. Participants may experience blurred vision for a period of time after the injection itself. Participants should not drive or use machinery until this has resolved.

Ocular fluid samples will be collected from the front part of the participant's eye using a small needle. Participants may experience a temporary decrease in pressure after aqueous humor collection. While rare, aqueous humor collection can cause eyes to develop infections inside and/or outside the eye (endophthalmitis, periocular, and/or corneal infections) or cataracts (cloudiness of the eye lens). Some participants can also develop bleeding inside the eye. Participants may experience blurred vision for a period of time after the procedure itself. Participants should not drive or use machinery until this has resolved.

Fluorescein angiography photographs (special pictures taken of the eyes to determine the extent of macular edema or swelling) require an injection of a dye into a vein in the participant’s arm. This may cause some discomfort at the needle site, and the injection of the dye could irritate the vein, or cause redness, swelling or redness at the injection site. It is possible that the vein or the skin around the site could be damaged. The most common side effects of the dyes are nausea and vomiting, and occasionally allergic reactions or feeling faint. The dye may also stain skin and urine, although this will only last for about a day. In rare cases, allergic reactions can be serious and include swelling of the voice box, difficulty breathing, and heart stopping (cardiac arrest).

Potential risks with dilation of the eyes are nausea, vomiting, dryness of the mouth, flushing, dizziness for a short time; allergic reaction; and sudden increase in pressure inside the eyeball.

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant or are currently breastfeeding cannot take part in this study.