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A study evaluating the effectiveness and safety of faricimab (RO6867461) in participants with polypoidal choroidal vasculopathy

Submission date 24/08/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 22/09/2022	**Overall study status** Ongoing	
Last Edited 30/01/2024	**Condition category** Eye Diseases	

Plain English summary of protocol

Background and study aims
Polypoidal choroidal vasculopathy (PCV) is a disease primarily affecting the blood vessels (choroidal vessels) under the light-sensitive membrane at the back of the eye (retina). This results in damage to the retina where the cells responsible for vision are present. Polypoidal injuries (lesions) commonly lead to significant subretinal bleeding (hemorrhage), often requiring aggressive therapy. Although the current treatment has demonstrated clinical benefit for patients with PCV, many limitations exist in understanding the disease. The burden of frequent injections, incomplete closure of polypoidal lesions, and the risk of the disease coming back (relapse) support the need to develop new therapeutic treatments. Faricimab is an experimental drug, which means health authorities have not approved
faricimab for the treatment outside of a clinical study. The aims of this study are to evaluate the effects, good or bad, of long-term use of faricimab in participants with PCV, and to determine how safe faricimab is when given to participants with PCV.

Who can participate?
People who are over 50 years of age and have a confirmed diagnosis of macular PCV

What does the study involve?
Participants may have to be a part of this study for about 2 years. The study will include:
1. Screening period: The screening period will last up to 28 days before the study starts. All participants will be screened to make sure they are a good fit for the study before the study begins.
2. Treatment period: This will consist of three treatment periods: a treatment initiation period (Day 1-Week 12), an individualized constant treatment interval period (Week 20-Weeks 44 or 48), and a personalized treatment interval (PTI) period (Weeks 44 or 48-Week 104). Participants will first receive four injections of faricimab 6 mg, injection in the study eye (intravitreal [IVT]) every 4 weeks. Thereafter participants will receive faricimab 6 mg injections into the study eye at a variable intervals, between every 4, 8, 12, 16, or 20 weeks, depending on the condition of the study eye.
Participants will have to visit the clinic about every 4 weeks during the study.

3. Follow-up period: Participants will have a check-up 4-5 weeks after the last dose of faricimab. Those who complete the treatment period of 104 weeks will be followed up at Week 108 for monitoring of side effects.

What are the possible benefits and risks of participating?
Participants may not receive any benefit from participating in this study, but the information learned in this study may help patients with similar conditions in the future. Participants may experience side effects from the study drug, and these can be mild to severe and can vary from person to person. As faricimab has had limited testing in humans, not all side effects are known at this time. The known side effects related to the study drug are listed below:

Common side effects:
1. Bleeding of the mucous membrane covering the white of the eye and inner lid (conjunctival hemorrhage)
2. Moving spots or dark shapes in the vision (vitreous floaters)
3. Temporary increase in fluid pressure inside the eye (increase in intraocular pressure)
4. Eye pain
5. The supporting membrane under the retina detaches and develops a hole, which can result in a reduction of vision (retinal pigment epithelium tear)

Uncommon side effects:
1. Eye irritation, discomfort, or itching
2. Increased production of tears
2. Bleeding into the jelly-like filling of the eye (vitreous hemorrhage)
4. Scratched cornea, damage to the clear layer of the eyeball that covers the iris (corneal abrasion)
5. Eye redness
6. Blurred vision
7. Inflammation of the gel-like substance inside the eye (vitritis)
8. Inflammation in the iris and its adjacent tissue in the eye (iritis, iridocyclitis, uveitis)
9. Foreign body sensation in the eye
10. Serious inflammation or infection inside the eye (endophthalmitis)
11. Temporary decrease in vision
12. Tearing of the retina

Rare side effects:
1. Separation of the retina from the underlying pigment cell layer (retinal detachment)

Potential risks associated with the study drug are listed below:

Potential systemic (non-ocular) side effects of faricimab:
1. Sickness caused by blood clots in the blood vessels (arteries) (arterial thromboembolic events) such as sudden interruption of blood flow in the brain which can cause paralysis and unconsciousness (strokes) and heart attack (myocardial infarctions) have been seen at a low rate in clinical trials with faricimab, and with anti-vascular endothelial growth factor eye drugs such as EYLEA (aflibercept) and LUCENTIS (ranibizumab).

Potential ocular side effects of faricimab:
1. As with all therapeutic proteins, there is the potential for a response of the immune system to the treatment with faricimab, which may show up as severe inflammation inside the eye.
2. As with all injections into the eye, there is a risk of developing traumatic clouding of the lens (cataract). This occurs when the injection needle directly injures the lens.

Risks associated with a few of the study procedures are listed below:
1. Injection into the eye: some participants develop increased pressure within the eye when a medication is injected into the eye. Participants with a history of damage to the nerve in the eye which is usually caused by high pressure in the eye (glaucoma) must be well-controlled on medication in order to participate in this study. While rare, some participants receiving injections of medication into their eye have developed infections inside and/or outside the eye (endophthalmitis and/or periocular infections), retinal detachment or cloudiness of the eye lens. Participants may experience blurred vision for a period of time after the injection itself.
2. Anesthetic procedure: participants may experience blurred vision, pain, or stinging in eye, watery eyes and redness, light sensitivity for a period after the numbing medication (anesthetic) is administered.
3. Indocyanin green angiography: indocyanin green is a dye needed for the procedure of indocyanin green angiography. Participants may experience discomfort at the needle site, and the injection of the dye could irritate the vein or cause redness or swelling at the injection site. The most common side effects of the dye are nausea and vomiting, and occasionally allergic reactions or feeling faint.
4. Fluorescein angiography: fluorescein is a dye needed for the procedure of fluorescein angiography Participants may experience discomfort at the needle site, and the injection of the dye could irritate the vein or cause redness or swelling at the injection site. The most common side effects of the dye are nausea and vomiting, and occasionally allergic reactions or feeling faint. The dye may also stain the skin and urine, although this will only last for about 1 day.
5. Eye drops: participants may experience blurred vision for a period of time after the eye drops used to dilate the pupil(s) for the various eye tests are administered. Participants should not drive or use machinery until this has resolved.
There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women must take precautions to avoid exposing an unborn child to the study drug. Women who are pregnant, become pregnant, or are currently breastfeeding, cannot take part in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (USA)

When is the study starting and how long is it expected to run for?
July 2021 to June 2026

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
MR43808

Study information

Scientific Title
A Phase IIIb/IV, multicenter, open-label, single-arm study to investigate the efficacy and safety of faricimab (RO6867461) in patients with polypoidal choroidal vasculopathy

Study objectives
The main aim of this study is to evaluate the efficacy, safety and durability of faricimab administered as intravitreal (IVT) injections in participants with polypoidal choroidal vasculopathy (PCV), including assessment of visual acuity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/04/2022, Ozawa Ophthalmology Medical Hospital Institutional Review Board (246-6 Yoshizawacho, Mito City, Ibaraki Prefecture, 310-0845, Japan; +81 (0)29 246 2111; chiken@kozawa-ganka.or.jp), ref: not applicable

Study design
Phase IIIb/IV multicenter open-label single-arm study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Polypoidal choroidal vasculopathy (PCV)

Interventions

Participants will receive faricimab 6 mg IVT, every 4 weeks (Q4W) from Day 1 up to Week 12. Thereafter, participants with protocol-defined active disease at Weeks 20 and 24 will continue to receive faricimab 6 mg IVT, every 8 weeks (Q8W) up to Week 44 and every 12 weeks (Q12W) up to Week 48, respectively. Participants without protocol-defined active disease at Weeks 20 and 24 will receive faricimab 6 mg IVT, at Week 28 and thereafter every 16 weeks (Q16W) up to Week 44. From Week 44, for participants on a Q8W or Q16W treatment interval, and Week 48 for those on a Q12W treatment interval, all participants will receive a personalized treatment interval (PTI) dosing regimen, ranging from Q8W to every 20 weeks (Q20W), based on disease activity, up to Week 104. At Week 108, participants will attend a follow-up visit following which their participation in the study will be considered as having been completed.

Intervention Type
Drug

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
Faricimab (RO6867461)

Primary outcome(s)
Best-corrected visual acuity (BCVA) measured on the Early Treatment Diabetic Retinopathy Study Visual Acuity (ETDRS VA) chart at a starting distance of 4 metres (m) at baseline, weeks 40, 44, and 48

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
28/06/2026

Eligibility

Key inclusion criteria
General inclusion criteria:
1. Age ≥50 years at the time of signing the informed consent form

Ocular inclusion criteria for study eye:
1. Have sufficiently clear ocular media and adequate pupillary dilatation to allow the acquisition of good-quality retinal images to confirm diagnosis
2. Confirmed diagnosis, by the investigator, of symptomatic macular PCV defined by the following:
2.1. Active macular polypoidal lesions shown by indocyanine green angiography (ICGA)
2.2. Presence of exudative or hemorrhagic features involving the macula as identified by the investigator using multimodal images
3. BCVA scores of 78-24 ETDRS letters, inclusive (20/32 to 20/320 approximate Snellen equivalent), using the ETDRS protocol and assessed at the initial testing distance of 4 m on study Day 1

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Sex
All

Total final enrolment
135

Key exclusion criteria
General exclusion criteria:
1. Treatment with investigational therapy (device, drug, or traditional medicine with the exception of vitamins and minerals) within 3 months prior to initiation of study treatment on study Day 1
2. Any major illness or major surgical procedure within 1 month before screening
3. Active cancer within the 12 months prior to study Day 1
4. Uncontrolled blood pressure, defined as systolic blood pressure >180 mmHg and/or diastolic blood pressure > 100 mmHg while the participant is at rest on study Day 1
5. Participants with a history of stroke (cerebral vascular accident) or myocardial infarction within 6 months prior to study Day 1
6. Participants with history of other disease, metabolic dysfunction, physical examination finding, or historical or current clinical laboratory findings giving reasonable suspicion of a condition that contraindicates the use of the investigational drug or that might affect the interpretation of the results of the study or renders the participant at high risk for treatment complications in the opinion of the investigator
7. Participants with history of severe allergic reaction or anaphylactic reaction to a biologic agent or known hypersensitivity to any component of the faricimab injection, study-related procedure preparations (including fluorescein and indocyanine green dyes), dilating drops, or any of the anesthetic and antimicrobial preparations used by a participant during the study
8. Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 28 days after the final dose of faricimab

Ocular exclusion criteria for both eyes:
1. Participants with history of idiopathic or autoimmune-associated uveitis in either eye
2. Participants with active ocular inflammation or suspected or active ocular or periocular infection in either eye on study Day 1

Ocular exclusion criteria for study eye:
1. Any history or presence of macular pathology unrelated to PCV affecting vision or contributing to the presence of macular hemorrhage, intraretinal fluid (IRF), or subretinal fluid (SRF)
2. Retinal pigment epithelial tear involving the macula on study Day 1
3. On fundus fluorescein angiography (FFA)/color fundus photograph (CFP):

3.1. Subretinal hemorrhage of > 4 macular photocoagulation study disc area and/or that involves the fovea
3.2. Fibrosis or atrophy of > 50% of the total lesion area and/or that involves the fovea
4. Any concurrent intraocular condition
5. Current vitreous hemorrhage on study Day 1
6. Uncontrolled glaucoma
7. Any prior or concomitant treatment for PCV or other retinal diseases, including, but not restricted to, IVT treatment (e.g., faricimab, anti-vascular endothelial growth factor (VEGF), steroids, tissue plasminogen activator, ocriplasmin, C3F8, air), periocular pharmacological intervention, argon laser photocoagulation, verteporfin photodynamic therapy, diode laser, transpupillary thermotherapy, or ocular surgical intervention.
8. Any other intraocular surgery (e.g., pars plana vitrectomy, glaucoma surgery, corneal transplant, or radiotherapy)
9. Prior periocular pharmacological or IVT treatment (including anti-VEGF medication) for other retinal diseases

Ocular exclusion criteria for fellow (non-study) eye:
1. Participants who have a non-functioning fellow (non-study) eye, defined as either BCVA of hand motion or worse, or no physical presence of non-study eye (i.e., monocular), at both the screening and study Day 1 visits will be excluded from study entry.

Date of first enrolment
15/11/2022

Date of final enrolment
27/12/2023

Locations

Countries of recruitment
China

Hong Kong

India

Japan

Korea, South

Malaysia

Singapore

Taiwan

Thailand

Study participating centre

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Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes