LAY CLINICAL TRIAL DESCRIPTION / PROTOCOL SYNOPSIS in LAY LANGUAGE

Roche Trial Number / Trial acronym (if available):
GR40550 / Pagoda

National Clinical Trial Number / EU Clinical Trial Number:
NCT04108156 / Not applicable

Trial title: Re-implantation substudy in association with study GR40550 (Pagoda): a multicenter, open-label study to evaluate the safety of re-implanting the port delivery system with ranibizumab in patients with diabetic macular edema

Lay study title:

A study to find out how safe it is to replace and refill an eye implant that releases medicine for people with diabetic macular oedema (DME) who were part of the Pagoda (GR40550) study

1. Why is this study needed?

Diabetic macular oedema (DME) is a condition where high blood sugar levels from diabetes cause fluid to leak into the central area at the back of the eye. This can cause blurry vision.

DME can be treated with anti-VEGF drugs like ranibizumab. Ranibizumab, given as an injection into the eye is approved by health authorities (like the U.S. Food and Drug Administration {FDA]) for the treatment of DME. These injections are needed as often as every 1 to 2 months. To reduce this frequency, a refillable device that is put into the eye (an eye implant) was designed that slowly releases ranibizumab over time. This implant, known as the Port Delivery System with ranibizumab, only needs to be refilled with ranibizumab about every 6 months. The eye implant, together with ranibizumab and the devices used to fill and refill the implant, are approved in the United States for the treatment of DME, neovascular age-related macular degeneration, also known as nAMD, and diabetic retinopathy (DR).

During the Pagoda (GR40550) study, in some participants, the eye implant became damaged, called 'septum dislodgement', and could no longer be refilled. The eye implant has been updated to lower the chance of damage to the implant. This study aims to test how safe it is to remove the damaged eye implant and to replace it with the new version. It will also test how safe it is to refill the new eye implant with ranibizumab.

2. Who can take part in the study?

People with DME can take part in the study if they took part in the main Pagoda study and either have a damaged eye implant in one of their eyes or have had the damaged eye implant replaced with a new eye implant during the Pagoda study.

People may not be able to take part in this study if they have a working eye implant, they have had the eye implant replaced before and require a new one, or they have an eye implant that is damaged in a way that is not septum dislodgement.

People who have a history of certain medical conditions or other eye diseases or who are taking certain treatments may not join the study. People who are pregnant, currently breastfeeding, or are planning to become pregnant during the study or within 1 year of their eye implant being refilled also cannot take part.

3. How does this study work?

Everyone will join 1 of 2 groups depending on whether they have already received a new implant in the main Pagoda study or not:

- Group 1 (have not received a new eye implant in the main study) will be given a new eye implant and refills every 6 months (2 refills in total).
- Group 2 (have already received a new eye implant in the main study) will receive refills every 6 months (up to 2 refills in total after receiving the new eye implant). Participants who had 2 scheduled refills in the main study will not be able to take part in this study.

If ranibizumab treatment is not working as well as expected, the study doctor may give extra ranibizumab, as needed, as an injection into the eye 1 and 2 months before the next eye implant refill is due.

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will contact participants a few days after each refill to check on their wellbeing. Participants will visit the study doctor every 3 months. The study doctor will check how well the treatment is working and any unwanted effects participants may have. If the participant leaves the study early, they will have a follow-up visit 1 month after their last refill or 3 months after receiving the new eye implant. At the final study visit, the study doctor will check on the participant's wellbeing and discuss whether the eye implant should be removed. If the eye implant is removed, participants will have 2 follow-up visits that week, then have monthly visits for 3 months. Total time of participation in the study will be 1 to 1 and a half years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main results measured in the study are the number and seriousness of unwanted effects, and the number of issues related to inserting, filling, refilling and/or removing the eye implant.

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other treatment options.

Risks associated with the study medicine, device, or procedures
Participants may have unwanted effects of the medicine, devices, or procedures used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular checks for any unwanted effects. The study doctor will take necessary measures if any unwanted effects are observed in the participants.

Ranibizumab
Participants will be told about the known unwanted effects of ranibizumab using the eye implant or as injections into the eye, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include pain or discomfort in the head, feeling that there is something in your eye, eye pain and irritation.

The study medicine(s) may be harmful to an unborn baby. Women must take precautions to avoid exposing an unborn baby to the study treatment.

Port Delivery System with Ranibizumab
Participants will be told about any known unwanted effects of the eye implant, and where relevant, also potential unwanted effects based on human and laboratory studies or knowledge of similar devices. The eye implant will be put into the eye under local anaesthetic (a medicine that numbs a specific area of the body, preventing the sensation of pain in that area).

Participants will be told about any known unwanted effects of the procedures involved in inserting, filling, refilling and removing (if needed) the eye implant, and, where relevant, potential unwanted effects based on human and laboratory studies or knowledge of similar procedures.