Design and Rationale of Elevatum: A Phase 4 Trial of Faricimab in Underrepresented Patients With Diabetic Macular Oedema

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Key Evidence Gap

Patients from certain minority groups have been historically underrepresented in clinical trials. We know that prevalence of diabetic retinopathy/diabetic macular oedema is overrepresented in these populations. The purpose of ELEVATUM is to improve our understanding of the treatment response of faricimab in underrepresented patients with macular oedema

Introduction

- Studies have shown that underrepresented populations, including Hispanics and Blacks, are more affected by diabetes and diabetic eye diseases[1,2] and the prevalence of diabetic retinopathy is 33.4% in Hispanic and 26.5% in Black patients vs 18.2% in Caucasian patients.[3]
- Hispanic and Black patients have worse baseline visual acuity and disease severity on starting anti-VEGF therapy for DMO vs Caucasian patients.[4] A retrospective study showed that VA improvements following 1 anti-VEGF injection were lowest in Black (26.7%) and Hispanic (39.4%) patients compared with Caucasian (50.0%) patients with DMO[5]
- The aim of Phase 4 ELEVATUM (NCT05224102) is to evaluate the treatment response and safety of faricimab in traditionally underrepresented, treatment-naïve patients with DMO. The population will consist of participants who self-identify as Black/African American, Hispanic/Latino American, Native American/Alaska Native/Native Hawaiian or other Pacific Islander; in addition, a cohort of participants will be enrolled in India and Kenya.

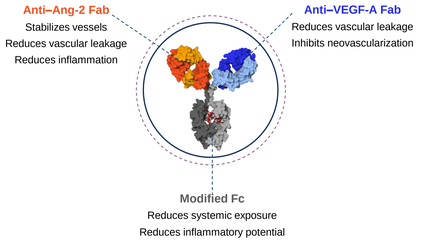
Methods

- ELEVATUM is a phase 4, multicenter, open-Label, single-arm study to investigate faricimab treatment response in treatment-naive, underrepresented patients with DMO.
- All patients will receive intravitreal faricimab 6.0 mg every 4 weeks (Q4W) up to week 20 (6 injections), then faricimab 6.0 mg Q8W up to week 52. Patients will return for the Week 56 safety follow-up visit after ≥28 days following their last study treatment.
- The primary outcome is change in BCVA from baseline at week 56.
- Other variables to be collected include diabetic retinopathy severity, multimodal imaging, aqueous humour samples and diabetic disease assessments, including HbA1c, lipid panel, urinalysis, genotyping (including apoliprotein-1), and hip and waist measurements. Patient-reported measures of diabetes disease burden (Diabetes Symptom Checklist-Revised, Diabetic Distress Scale, International Physical Activity Questionnaire and Mediterranean Diet Adherence Screener) and social determinants of health (primary language, housing status, education, employment, insurance and zip codes) will also be assessed.

Conclusions

- The ELEVATUM trial is the first inclusive research clinical trial for Ophthalmology. It is designed to improve understanding of the use of faricimab in DMO in underrepresented patients and the associated social, health, and operational barriers that limit trial recruitment and retention in these populations
- ELEVATUM's impact spans well beyond adding important information in our patient populations. This study will improve the understanding of barriers and challenges patients from under-represented communities face in clinical trials that limit their access and participation as these patients are systematically underrepresented and in many cases disproportionately affected by the disease.

1. Faricimab Targets Two Disease Pathways via Inhibition of Ang-2 and VEGF-A to Improve Vascular Stability[6]

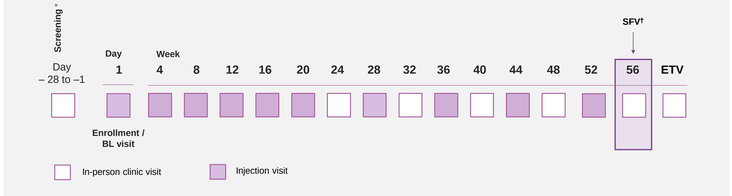


- **YOSEMITE** and **RHINE** were **phase 3**, randomized, double-masked, **active comparator–controlled trials**
- Designed to assess the **efficacy**, **safety,** and **durability of faricimab**
- In **treatment-naïve and previously treated patients** with center-involving **DMO** (CST ≥ 325 µm)[a]
- Comparable 1-year **BCVA gains** and **improved anatomic outcomes** with faricimab **up to Q16W** versus aflibercept Q8W were **maintained through year 2**[7]

YOSEMITE: NCT03622580; RHINE: NCT03622593. [a]CST was measured as the distance from the internal limiting membrane to Bruch's membrane. CrossMAb molecule representative of faricimab.
Ang-2, angiopoietin-2; BCVA, best-corrected visual acuity; CST, central subfield thickness; DMO, diabetic macular oedema; Fab, fragment antigen binding; Fc, fragment crystallizable; Q8W, every 8 weeks; Q16W, every 16 weeks; VEGF-A, vascular endothelial growth factor-A.

2. Study Design

- **An open-label, single-arm, phase 4 study in patients with DMO** (N = ~120 across 40 sites)
- **Primary Endpoint: Change in BCVA from baseline at week 56**



Screening performed within 28 days preceding the BL visit (i.e., day of first study treatment). If requiring > 28 days, the screening period may be extended by up to 5 business days. † A patient is considered to have completed the study if he/she has completed the SFV at Week 56. Patients who discontinue from the study or treatment early (before week 56) should return for an ETV after ≥ 28 days have elapsed following their last study treatment.
BCVA, best-corrected visual acuity; BL, baseline; DMO, diabetic macular oedema; ETV, early termination visit; SFV, safety follow-up visit.

3. Key Eligibility Criteria

Key General Inclusion Criteria

✓ **Patients ≥ 18 years** who self-identify as:
- **Black/African American (~45%)**
- **Hispanic/Latino American (~45%)**
- **Native American/Alaska Native/Native Hawaiian** or other **Pacific Islander (~10%)**

✓ Patients with **type 1 or 2 diabetes mellitus** who are regularly using insulin, other injectable drugs, or oral anti-hyperglycemic agents
- **HbA1c ≤ 10%** during screening (**up to 20%** of enrolled patients **may have HbA1c up to 12%**)

Key Ocular Inclusion Criteria for the Study Eye

✓ Patients* with **DMO without prior** IVT **anti-VEGFs** or any IVT or periocular **corticosteroids**

✓ BCVA of **20–73** ETDRS **letters** (~20/40–20/400 Snellen) (both inclusive) at the initial testing distance of 4 meters at baseline (day 1)

✓ CST of **≥ 325 µm**†

Key Ocular Exclusion Criteria for the Fellow Eye

- Ongoing treatment with **brolucizumab** or **bevacizumab**

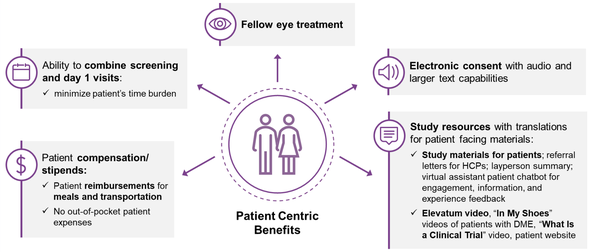
† CST measured from inner limiting membrane to Bruch's membrane.
BCVA, best-corrected visual acuity; CST, central subfield thickness; DMO, diabetic macular oedema; ETDRS, Early Treatment Diabetic Retinopathy Study; HbA1c, hemoglobin A1c; IVT, intravitreal; VEGF, vascular endothelial growth factor.

4.Key Study Assessments



AH, aqueous humor; DDS, diabetic distress scale; DSC-R, Diabetes Symptom Checklist-Revised; ETDRS, Early Treatment Diabetic Retinopathy Study; FA, fluorescein angiography; HbA1c, hemoglobin A1c; IPAQ-SF, International Physical Activity Questionnaire-short Form; MEDAS, Mediterranean Diet Adherence Screener; NEI VFQ-25, National Eye Institute Visual-Functioning Questionnaire-25; PRO, patient-reported outcomes; SD-OCT-A, spectral-domain optical coherence tomography angiography; SS-OCT, swept-source optical coherence tomography; SS-OCT-A, swept-source optical coherence tomography angiography; VA, visual acuity; WGS, whole genome sequencing.

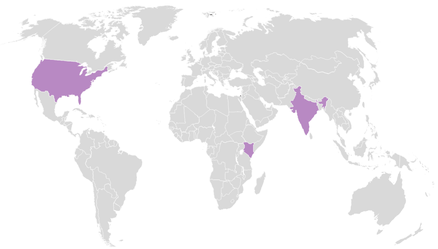
5.Study Level Patient Centric Benefits



DMO, diabetic macular oedema; HCP, health care provider.

6. Global Site Map

The ELEVATUM trial started in the USA and has been extended to other countries with populations underrepresented in clinical trials like Africa and India



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Financial Disclosures
- AWS: Consultant: Allergan/AbbVie, Alimera, Bausch + Lomb, DORC, EyePoint, Iveric, Regeneron; Consultant, Research: Roche/Genentech
- MA, JC, MY, IS: Employee: Genentech, Inc.

Study and Product Disclosures
- Faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema in multiple countries worldwide and is not currently approved for use outside these indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and writing assistance, which was provided by Saima Khokhar, Medical Affairs Partner of Roche Products Ltd, UK