Faricimab causes rapid and sustained intraocular suppression of Ang-2 and VEGF-A for up to 16 weeks in nAMD and DMO

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On behalf of the TENAYA and LUCERNE, and YOSEMITE and RHINE Investigators

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Key Clinical Question

To characterise the extent and duration of suppression of Ang-2 and VEGF-A in the Aqueous Humor (AH) of patients treated with faricimab

Introduction

- Faricimab is a bispecific antibody designed to inhibit angiopoietin-2 (Ang-2) and vascular endothelial growth factor A (VEGF-A), promote vascular stability, and improve outcomes in neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DMO)
- Optional aqueous humor (AH) samples were collected from patients in randomized, double-masked, active comparator–controlled, phase 2/3 trials in nAMD (AVENUE [NCT02484690], STAIRWAY [NCT03038880], TENAYA [NCT03823287], and LUCERNE [NCT03823300]) and DMO (BOULEVARD [NCT02699450], YOSEMITE [NCT03622580], and RHINE [NCT03622593])
- The goal of the work presented here was to characterise the effect of faricimab on the dynamics of Ang-2 and VEGF-A suppression

Methods

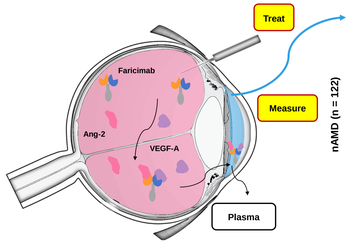
- Samples collected at multiple time points from patients with nAMD or DMO in phase 2 and 3 trials
- Based on:
  - 1025 Ang-2 observations from 225 patients
  - 1345 VEGF-A observations from 302 patients
  - 1095 faricimab observations from 284 patients
- Free Ang-2, VEGF-A and faricimab concentrations measured using validated bioanalytical assays
  - AH Concentrations, LLOQ: Ang-2, 4.04 pg/mL; VEGF-A, 1.46 pg/mL; faricimab,7.8ng/mL
- A popPKPD model was developed to characterize the extent and duration of intraocular target suppression, using a pooled PK and PD dataset from faricimab-treated patients with nAMD or DMO

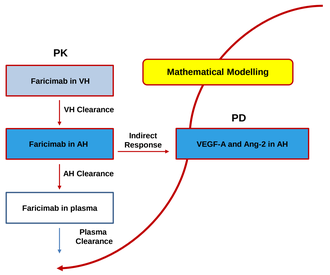
Conclusions

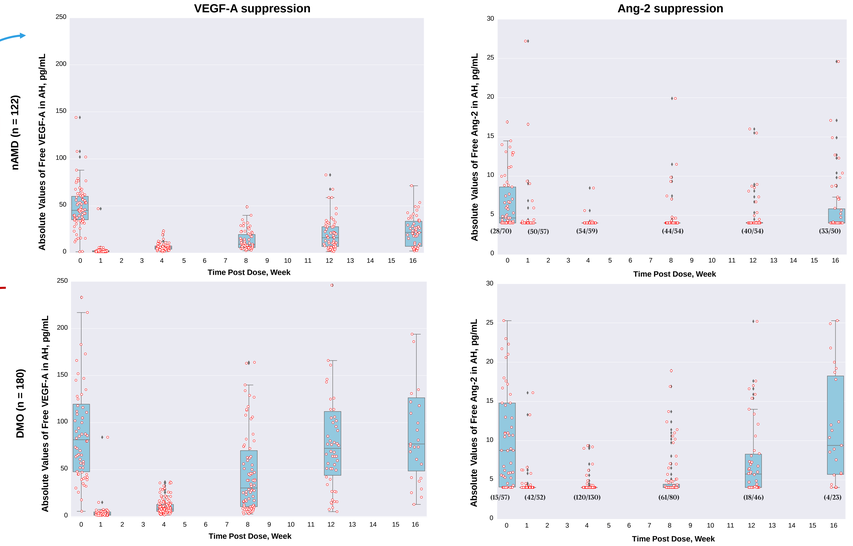
- In Phase 3 Clinical trials, dual Ang-2/VEGF-A inhibition in faricimab-treatment patients provided durable visual gains with Q16W dosing in ~60% of patients'
- Rapid and sustained suppression of VEGF-A and Ang-2 were observed in faricimab-treated patients with nAMD or DMO
- The popPKPD model predicts Ang-2 concentrations remain below baseline through at least 16 weeks post dose
- These findings are consistent with faricimab clinical durability data

1. Observed Target Suppression of VEGF-A and Ang-2 from AH Samples of Faricimab-treated Patients

- AH and plasma samples from consenting patients at multiple time points, producing a large and high-quality dataset
- Rapid and sustained suppression of VEGF-A and Ang-2 was observed in faricimab-treated patients with nAMD or DMO
- ~80% or more of the Ang-2 concentrations were BLQ within 8 weeks post dose
- A 3-compartment linear PK model linked to an indirect response PD model was developed to describe the dynamics of Ang-2 and VEGF-A suppression in patients with nAMD or DMO





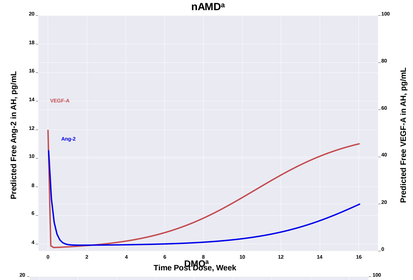


Ang-2 concentrations BLQ are represented at the lower limit of quantification value. Numbers in parentheses represent the number of BLQ observations/total number of observations at that time point.
AH, aqueous humor; Ang-2, angiopoietin-2; BLQ, below limit of quantification; DMO, diabetic macular oedema; nAMD, neovascular age-related macular degeneration; PD, pharmacodynamics; PK, pharmacokinetics; VEGF, vascular endothelial growth factor; VEGF-A, vascular endothelial growth factor-A; VH, vitreous humor.

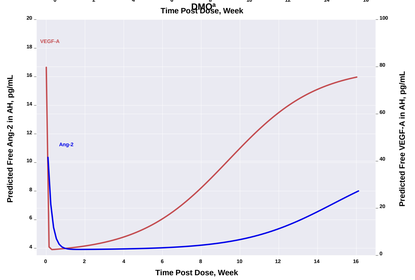
2. Predicted Dynamics of Intraocular AH Ang-2 and VEGF-A Suppression in Faricimab-treated Patients

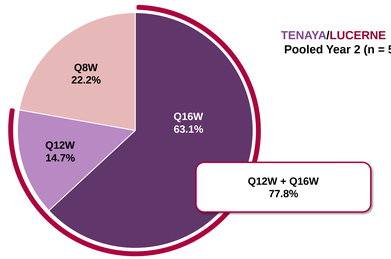
- In the TENAYA and LUCERNE nAMD trials and also in the YOSEMITE and RHINE DMO trials, ~80% of patients achieved = Q12W dosing with faricimab at year 2
- Median **VEGF-A** concentrations returned close to baseline ~16 weeks post dose
- Median **Ang-2** concentrations remained below baseline through at least 16 weeks post dose

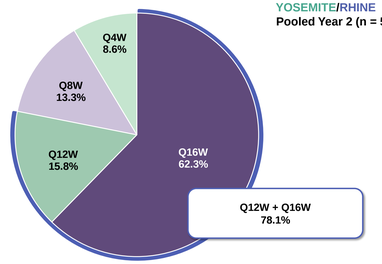
Predicted Dynamics of Intraocular VEGF-A and Ang-2 Suppression Through Week 16 Post Dose (nAMD)



Predicted Dynamics of Intraocular VEGF-A and Ang-2 Suppression Through Week 16 Post Dose (DMO)







- [a]The graphs are median AH, Ang-2, and VEGF-A concentrations over time derived from the popPKPD model by disease population. Model prediction based on 78-year old male with body weight of 79 kg and non-ADA.
- [b]Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at that visit. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Interval at week 112 is calculated using data recorded at week 108. ADA, anti-drug antibody; AH, aqueous humor; Ang-2, angiopoietin-2; DMO, diabetic macular oedema; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; Q8W, every 8 weeks, Q12W, every 12 weeks; Q16W, every 16weeks; VEGF-A, vascular endothelial growth factor-A.

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References

1. CrossMAb molecule representative of faricimab. Regula JT et al. EMBO Mol Med. 2016;8(11):1265-1288, with erratum in Regula JT et al. EMBO Mol Med. 2019;11(5):e10666.

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- KB, CD: Employee: F. Hoffmann-La Roche Ltd.
- IS: Employee: Genentech, Inc.

Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular edema 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
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