Personalised Treatment Interval (PTI) Dynamics Over 2 Years in the Phase 3 YOSEMITE and RHINE Trials of Faricimab in Diabetic Macular Oedema

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Introduction

- Dual inhibition of the angiopoietin-2 and vascular endothelial growth factor-A (VEGF-A) pathways with faricimab may promote vascular stability and extend treatment durability beyond current anti-VEGF therapies for diabetic macular oedema (DMO)[1-3]
- In the phase 3 YOSEMITE and RHINE trials, treat-and-extend–based personalised treatment interval (PTI) dosing up to every 16 weeks (Q16W) was designed to test the durability of faricimab and optimise dosing intervals for patients with DMO[3]

Methods

- YOSEMITE (NCT03622580) and RHINE (NCT03622593) were randomised, double-masked, phase 3 trials of faricimab in patients with centre-involving DMO (central subfield thickness [CST] ≥ 325 µm; best-corrected visual acuity [BCVA] 25–73 letters)
- Patients were randomised 1:1:1 to faricimab 6.0 mg Q8W, faricimab 6.0 mg per PTI or aflibercept 2.0 mg Q8W
- In the PTI arms, patients received faricimab Q4W until CST < 325 µm was achieved at or after week 12
- Once achieved, dosing intervals could be extended by 4 weeks (up to Q16W), maintained or reduced by 4 or 8 weeks (as low as Q4W), based on CST and BCVA change at active dosing visits
- Dosing intervals in the faricimab PTI arms were assessed through week 96

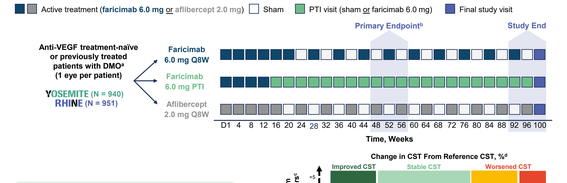
Safety

- Faricimab was well tolerated through study end, with an acceptable safety profile comparable with aflibercept
- Rates of intraocular inflammation were low across treatment arms, and no cases of retinal vasculitis or occlusive retinal vasculitis were reported
- The RHONE-X (NCT04432831) long-term extension study will continue to evaluate the safety of faricimab in patients with DMO

Conclusions

- Treat-and-extend–based PTI dosing in the YOSEMITE and RHINE trials was effectively used to optimise faricimab treatment intervals to the heterogeneous needs of patients with DMO
- The majority of patients in the faricimab PTI arms achieved Q12W or Q16W dosing at week 96
- Most patients who achieved Q12W or Q16W dosing at week 52 maintained extended dosing through week 96, while also maintaining robust vision gains and anatomic improvements
- These data support the extended durability of dual angiopoietin-2 and VEGF-A inhibition with faricimab for the treatment of DMO

1. YOSEMITE/RHINE Study Design and PTI Regimen

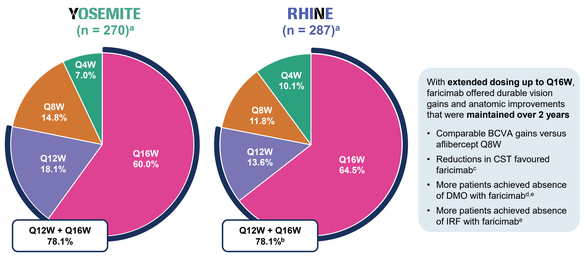


Personalised Treatment Interval (PTI)

Treat-and-extend–based dosing regimen
Intervals adjusted (**from Q4W up to Q16W**) based on CST and BCVA change at active dosing visits

[a] Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrolment. [b] Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52 and 56. [c] Reference BCVA was defined as the mean of the 3 best BCVA values achieved at any prior active dosing visit. [d] Reference CST was defined as the CST value when the original reference value (CST < 325 µm) was achieved. Reference CST was adjusted if CST demeaned by > 10% from the previous reference CST for 2 consecutive active dosing visits and the values obtained were within 30 µm. The CST value obtained at the latter visit served as the new reference CST. BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DMO, diabetic macular oedema; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q16W, every 16 weeks; VEGF, vascular endothelial growth factor.

2. Durable Efficacy Was Achieved With Q16W Dosing in ≥ 60% of Patients in the Faricimab PTI Arms at Week 96

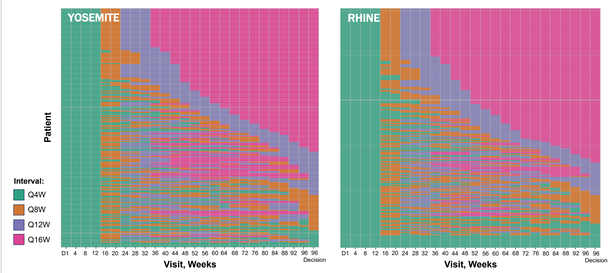


With **extended dosing up to Q16W**, faricimab offered durable vision gains and anatomic improvements that were **maintained over 2 years**

- Comparable BCVA gains versus aflibercept Q8W
- Reductions in CST favoured faricimab[c]
- More patients achieved absence of DMO with faricimab[d,e]
- More patients achieved absence of IRF with faricimab[e]

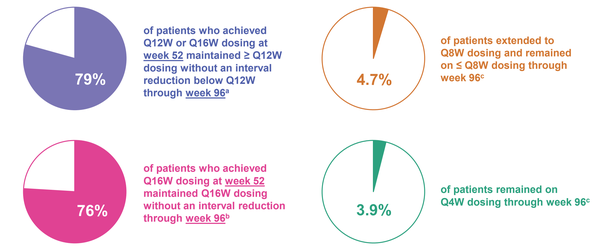
[a] Analyses included patients in the faricimab PTI arms who had not discontinued the study at the week 96 visit. Treatment interval at week 96 was defined as the treatment interval decision made at that visit. [b] Sum of Q12W and Q16W percentages shown; calculated proportion of patients who achieved Q12W or Q16W dosing at week 96 is 78.049%. [c] In general, patients receiving faricimab achieved greater reductions in CST over time compared with aflibercept (not a statistically significant difference). [d] Absence of DMO was defined as CST < 325 µm, measured as the distance from the internal limiting membrane to Bruch's membrane. [e] In general, a numerically greater proportion of patients receiving faricimab achieved absence of DMO or absence of IRF over time compared with aflibercept.
BCVA, best-corrected visual acuity; CST, central subfield thickness; DMO, diabetic macular oedema; IRF, intraretinal fluid; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

3. Dosing Intervals in the Faricimab PTI Arms Through Week 96



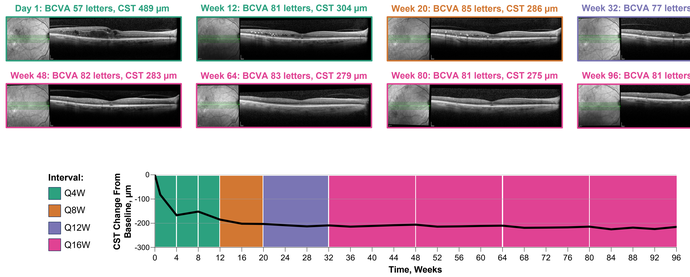
Analyses included patients in the faricimab PTI arms who had not discontinued the study at the week 96 visit (YOSEMITE, n = 270; RHINE, n = 287).
Treatment interval at a given visit is shown as the interval at the start of the visit. The week 96 decision (recorded/calculated at week 96) is shown in the last column.
D, day; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

4. Most Patients Who Achieved Q12W or Q16W Dosing at 1 Year Maintained Extended Dosing Through Year 2



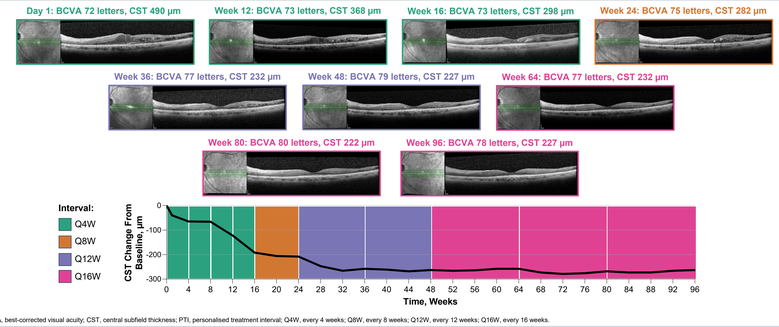
[a] Percentage is based on the number of patients in the faricimab PTI arms who achieved Q12W or Q16W dosing at week 52 and had not discontinued the study at the week 96 visit (YOSEMITE/RHINE pooled, n = 406).
[b] Percentage is based on the number of patients in the faricimab PTI arms who achieved Q16W dosing at week 52 and had not discontinued the study at the week 96 visit (YOSEMITE/RHINE pooled, n = 291).
[c] Percentage is based on the number of patients in the faricimab PTI arms who had not discontinued the study at the week 96 visit (YOSEMITE/RHINE pooled, n = 557).
PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

5. PTI Case 1: Rapid Extension to Q16W Dosing, Which Was Maintained Through Year 2



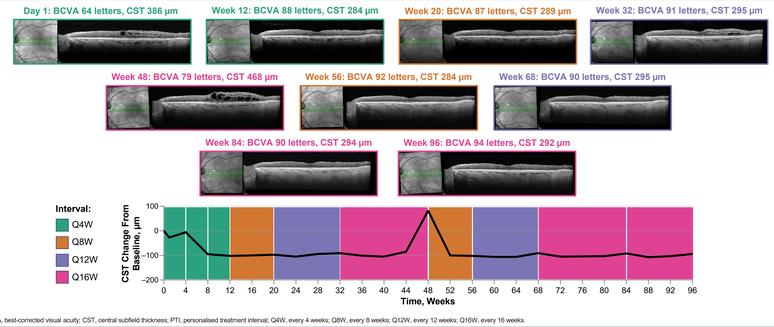
BCVA, best-corrected visual acuity; CST, central subfield thickness; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

6. PTI Case 2: Gradual Extension to Q16W Dosing, Which Was Maintained Through Year 2



BCVA, best-corrected visual acuity; CST, central subfield thickness; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

7. PTI Case 3: Rapid Extension to Q16W Dosing Followed by Interval Reduction, Extension to Q16W Dosing and Maintenance Through Year 2



BCVA, best-corrected visual acuity; CST, central subfield thickness; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

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Financial Disclosures

- IAP: Consultant/Lecture Fees: Adverum, Allergan, Apellis, Bayer, Biogen, Novartis, Roche
- GJJ: Consultant: Adverum, Annexon, EyePoint, Gemini, Iveric Bio, Novartis, Ripple, Roche/Genentech, Inc.
- BSG: Consultant: Bayer, Novartis, Roche; Research Support: Digital Diagnostics
- FA, KA, AC, ZH: Employee: Genentech, Inc.
- NJ: Employee: Roche Products Ltd.

Study and Product Disclosures

- Faricimab has been approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema in the United States and Japan, and is currently being studied for the treatment of macular oedema due to retinal vein occlusion. Please note that faricimab has not been approved for use outside these countries, or for use outside its approved indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation

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