Faricimab Treat-and-Extend for Diabetic Macular Edema (DME): Two-Year Results from the Randomized Phase 3 YOSEMITE and RHINE Trials

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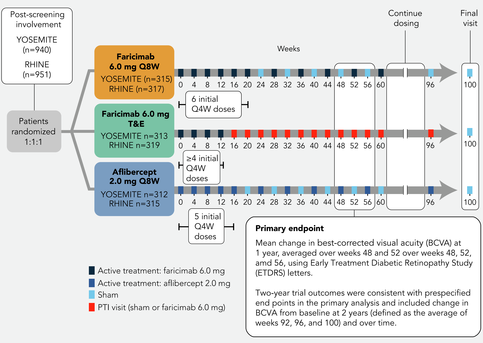
To evaluate the longer-term 2-year efficacy, durability, and safety of dual inhibition of angiopoietin-2 and vascular endothelial growth factor (VEGF) pathways with intravitreal faricimab according to a personalized treat-andextend (T&E)-based regimen with up to every-16-week dosing in the YOSEMITE and RHINE phase 3 trials of diabetic macular edema (DME). At 1 year, YOSEMITE and RHINE each met their primary end point; adjusted mean best-corrected visual acuity (BCVA) changes from baseline with faricimab every 8 weeks and T&E up to every-16-week dosing ranged between 10.8 and 11.8.

Adults with vision loss due to center-involving DME were randomized, double-masked, and assigned to non-inferiority trials across 353 sites worldwide in 31 participating countries. Efficacy analyses were based on the intention-to-treat population, grouped by treatment arm at randomization



Faricimab 6.0 mg Q8W
The 8-week groups received intravitreal faricimab 6.0 mg every 4 weeks up to week 20 (six injections), then fixed dosing every 8 weeks up to week 96.

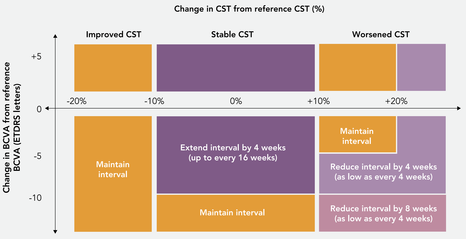
Faricimab 6.0 mg T&E
Patients in the personalized treatment interval (PTI) groups received faricimab 6.0 mg every 4 weeks until they first reached a central subfield thickness (CST) of less than 325 µm at or after week 12. Once achieved, treatment intervals were extended to every 8 weeks, then could be maintained, extended by 4 weeks (up to every 16 weeks), or reduced by 4 weeks or 8 weeks (as low as every 4 weeks) based on prespecified CST and BCVA criteria at active dosing visits. The PTI algorithm was designed to imitate treatment patterns in clinical practice; therefore, CST and BCVA assessments at sham injection visits were not used to determine dosing intervals for the PTI groups. PTI was designed to test the durability of faricimab using methods similar to those common in clinical practice, and is the first individualized treatment regimen to be examined in a double-masked manner.

Aflibercept 2.0 mg Q8W
The 8-week groups received intravitreal aflibercept 2.0 mg every 4 weeks up to week 16 (five injections), then fixed dosing every 8 weeks up to week 96.

To maintain masking, all patients attended study visits every 4 weeks and received sham injections at non-active dosing visits.

Changes to dosing intervals in the faricimab T&E arm were based on prespecified CST and BCVA criteria at active dosing visits

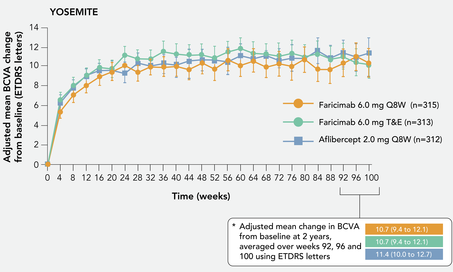
Faricimab treat-and-extend algorithm in the YOSEMITE and RHINE trials



Reference CST was defined as the CST value when the initial CST threshold criteria were met (CST < 325 µm at or after the week 12 study visit).
Reference BCVA was defined as the mean of the 3 best BCVA scores obtained at any previous active dosing visit.

In YOSEMITE and RHINE trials, noninferior year 1 visual acuity gains were maintained through year 2

Adjusted mean change in BCVA from baseline through week 100 in YOSEMITE AND RHINE*



* Adjusted mean change in BCVA from baseline at 2 years, averaged over weeks 92, 96 and 100 using ETDRS letters

10.7 (9.4 to 12.1)	
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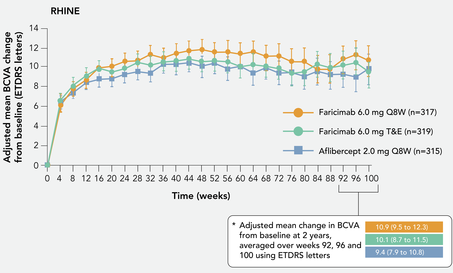
11.4 (10.0 to 12.7)	

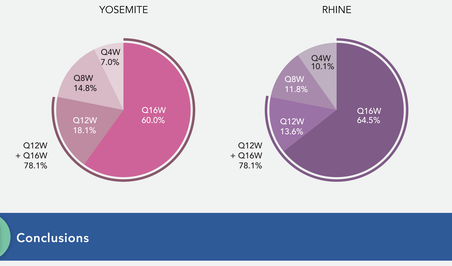


* Adjusted mean change in BCVA from baseline at 2 years, averaged over weeks 92, 96 and 100 using ETDRS letters

10.9 (9.5 to 12.3)	
10.1 (8.7 to 11.5)	
9.4 (7.9 to 10.8)	

The durability of faricimab was further improved during year 2 of YOSEMITE and RHINE, with greater patient proportions in the T&E arms extending their dosing while maintaining visual acuity gains and anatomic benefits versus aflibercept

Proportion of patients in the faricimab T&E arms who achieved every-4-week, every-8-week, every-12-week, or every-16-week dosing at week 96



Conclusions

Overall, faricimab was well tolerated, with a safety profile comparable with that of aflibercept.

Clinically meaningful visual acuity gains from baseline, anatomic improvements, and extended durability with intravitreal faricimab up to every 16 weeks were maintained through year 2.

Faricimab given as a personalized T&E-based dosing regimen supports the role of dual angiopoietin-2 and VEGF-A inhibition to promote vascular stability and to provide durable efficacy for patients with DME.