Efficacy, Durability, and Safety of Faricimab in Asian Patients With Diabetic Macular Oedema: 1-Year Subgroup Analysis of the Phase 3 YOSEMITE and RHINE Trials

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Key Clinical Question

What is the longer-term efficacy, durability and safety of faricimab in the Asian country subgroup vs the non-Asian country subgroup of patients with diabetic macular oedema (DMO)?

Introduction

- Dual inhibition of Ang-2 and VEGF-A with faricimab may result in stabilized vessels and reduced neovascularisation, leading to durable efficacy when treating retinal diseases[1]
- YOSEMITE (NCT03622580; N = 940) and RHINE (NCT03622593; N = 951) are identical, randomised, double-masked, active comparator-controlled trials of faricimab in treatment-naïve and previously anti-VEGF–treated patients with DMO[2]
- This poster presents 1-year results from the Asian subgroup analysis of the 2 phase 3 YOSEMITE and RHINE trials of faricimab in diabetic macular oedema

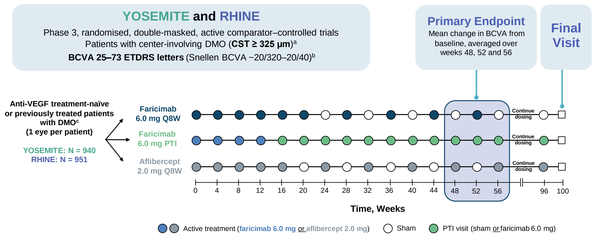
Methods

- In the pooled YOSEMITE and RHINE trials, 144 patients with DMO were from study sites in China, Taiwan, Hong Kong, Japan, South Korea, Singapore and Thailand and were classified as the Asian country subgroup.
- The non-Asian population included patients enrolled from all other participating countries and were of white, black or African American, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and Hispanic or Latin ethnicity.
- Patients with center-involving DMO (defined as a central subfield thickness of 325 µm or more) and BCVA of 20/40 or worse were included in these studies.
- Patients were randomised equally to faricimab every 8 weeks after 6 monthly doses, faricimab according to a personalised treatment interval (or PTI) with adjustable dosing up to every 16 weeks or aflibercept every 8 weeks per its globally approved label.
- The primary endpoint was mean change in BCVA from baseline at 1 year, averaged over weeks 48, 52 and 56.

Conclusions

- In conclusion, 1-year results from the phase 3 YOSEMITE and RHINE trials showed that faricimab every 8 weeks or PTI offered comparable vision gains versus aflibercept every 8 weeks, while also demonstrating anatomic improvements and the potential for extended dosing up to every 16 weeks.
- In the Asian country subgroup, initial BCVA gains were sustained for the majority of patients in the faricimab treatment arms.
- The durability of faricimab in the Asian country subgroup was consistent with the non-Asian country subgroup, with ~50% of patients in the Asian country subgroup on Q16W dosing at week 52 and >70% of patients on Q12W dosing or longer.
- Reductions in CST over time were comparable between Asian and non-Asian country subgroups. At baseline, 53–72% of patients across treatment arms in the Asian country subgroup had absence of SRF, compared with 63–66% of patients in the non-Asian country subgroup, this increased to ~100% across treatment arms and subgroups at week 16 and was maintained through week 56.
- Overall, faricimab was well tolerated through week 56, with a safety profile that was generally similar between Asian and non-Asian country subgroups.

1. YOSEMITE and RHINE Investigated Faricimab Q8W or Treat-and-Extend-Based PTI Dosing With Up to Q16W Intervals



[a]CST was measured as the distance from the internal limiting membrane to Bruch's membrane. [b]BCVA was measured using the ETDRS visual acuity chart at a starting distance of 4 m. [c]Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrolment. BCVA, best-corrected visual acuity; CST, central subfield thickness; DMO, diabetic macular oedema; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; VEGF, vascular endothelial growth factor.

2. Baseline characteristics were balanced across treatment arms and subgroups

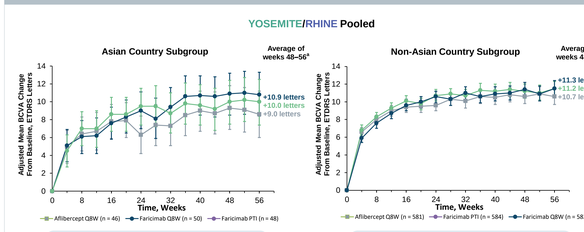
YOSEMITE/RHINE Pooled

	Asian Country Subgroup N = 144			Non-Asian Country Subgroup N = 1747		
Characteristic	Faricimab Q8W n = 50	Faricimab PTI n = 48	Aflibercept Q8W n = 46	Faricimab Q8W n = 582	Faricimab PTI n = 584	Aflibercept Q8W n = 581
Age, years, mean (SD)[a]	62.0 (10.0)	60.7 (10.7)	63.8 (7.6)	62.1 (9.8)	62.3 (10.0)	62.1 (10.0)
Female, n (%)	20 (40.0%)	20 (41.7%)	21 (45.7%)	231 (39.7%)	216 (37.0%)	242 (41.7%)
BCVA, ETDRS letters, mean (SD)	60.7 (11.2)	61.2 (8.7)	60.2 (9.0)	62.0 (9.9)	62.2 (9.9)	62.3 (9.5)
CST, µm, mean (SD)[b]	483.4 (131.6)	483.6 (142.5)	493.3 (119.7)	478.8 (128.2)	478.1 (128.0)	479.9 (131.1)
Previously anti-VEGF treated, n (%)	13 (26.0%)	10 (20.8%)	10 (21.7%)	127 (21.8%)	122 (20.9%)	127 (21.9%)
Baseline DR severity status, n (%)						
DR questionable, mild to moderate NPDR (ETDRS-DRSS level 10/12, 14/20, 35, 43)	25 (50.0%)	22 (45.8%)	25 (54.3%)	332 (57.0%)	343 (58.7%)	337 (58.0%)
Moderately severe and severe NPDR (ETDRS-DRSS level 47, 53)	24 (48.0%)	22 (45.8%)	17 (37.0%)	198 (34.0%)	176 (30.1%)	191 (32.9%)
PDR (ETDRS-DRSS level 61, 65, 71/75)	1 (2.0%)	3 (6.3%)	3 (6.5%)	41 (7.0%)	55 (9.4%)	35 (6.0%)
Cannot grade (ETDRS-DRSS level 90)	0	1 (2.1%)	1 (2.2%)	6 (1.0%)	9 (1.5%)	11 (1.9%)
Missing	0	0	0	5 (0.9%)	1 (0.2%)	7 (1.2%)

Results are presented for the intent-to-treat population. [a]Age at randomisation. [b]CST was measured as the distance from the internal limiting membrane to Bruch's membrane. BCVA, best-corrected visual acuity; CST, central subfield thickness; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study;NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PTI, personalised treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.

3. Initial BCVA gains were sustained in the faricimab arms.

YOSEMITE/RHINE Pooled



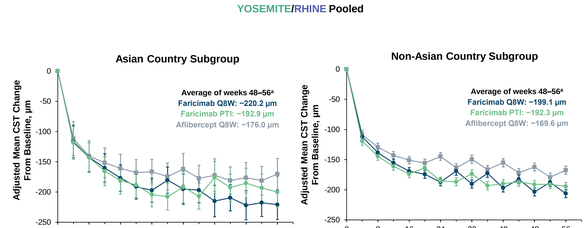
Treatment difference vs aflibercept Q8W at 1 year[a] (ETDRS letters), mean (95% CI)
Faricimab Q8W: +1.9 (−1.4, +5.3)
Faricimab PTI: +1.1 (−2.3, +4.4)

Treatment difference vs aflibercept Q8W at 1 year[a] (ETDRS letters), mean (95% CI)
Faricimab Q8W: +0.6 (−0.5, +1.7)
Faricimab PTI: +0.5 (−0.6, +1.7)

[a]Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52 and 56. Results are based on a mixed-model for repeated measures analysis. Error bars represent 95% CIs. BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks.

4. Reductions in CST over time were comparable between Asian and non-Asian country subgroups

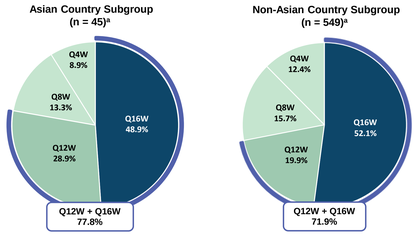
YOSEMITE/RHINE Pooled



[a]Adjusted mean CST change from baseline at 1 year, averaged over weeks 48, 52 and 56. Results are based on a mixed-model for repeated measures analysis. Error bars represent 95% CIs. CST, central subfield thickness; PTI, personalisedtreatment interval; Q8W every 8 weeks; Q16W, every 16 weeks.

5. Durable visions gains achieved with >70% of patients in the faricimab PTI arm.

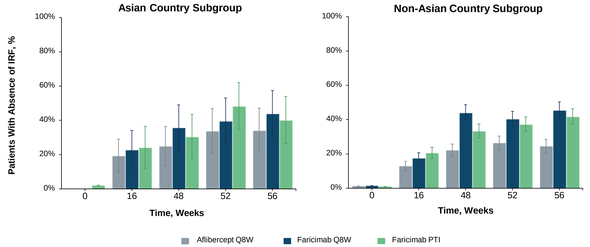
YOSEMITE/RHINE Pooled



[a]Analyses included patients in the faricimab PTI arm who had not discontinued the study at the week 52 visit.Treatmentinterval at week 52 was defined as the treatment interval decision made at that visit. PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

6. More than 40% of patients achieved absence of IRF measured in the central 1-mm diameter of the ETDRS grid in the faricimab arms at week 56

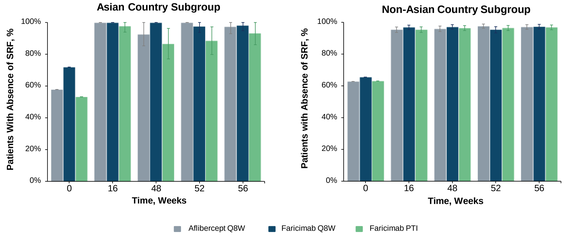
YOSEMITE/RHINE Pooled



IRF was measured in the central 1-mm diameter of the ETDRS grid. Weighted proportions were estimated using the CMH method; weighted proportions for the aflibercept Q8W arms are presented for the faricimab Q8W versus aflibercept Q8W comparison. Baseline values (defined as the last available measurement obtained on or before randomisation) are based on observed data. Error bars represent 95% CIs; estimates < 0% or > 100% were imputed as 0% or 100%, respectively. Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively. CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus 2019; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; PTI, personalised treatment interval; Q8W every 8 weeks.

7. Rates of absence of SRF measured in the central 1-mm diameter of the ETDRS grid through to year 1 were high across treatment arms and subgroups.

YOSEMITE/RHINE Pooled



SRF was measured in the central 1-mm diameter of the ETDRS grid. Weighted proportions were estimated using the CMH method; weighted proportions for the aflibercept Q8W arms are presented for the faricimab Q8W versus aflibercept Q8W comparison. Baseline values (defined as the last available measurement obtained on or before randomisation) are based on observed data. Error bars represent 95% CIs; estimates < 0% or > 100% were imputed as 0% or 100%, respectively. Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively.CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus 2019; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalised treatment interval; Q8W, every 8 weeks; SRF subretinal fluid.

8. Faricimab was well tolerated through week 56

	Asian Country Subgroup N = 144			Non-Asian Country Subgroup N = 1743		
AEs Through Week 56, Patients With ≥ 1 AE, n (%)[a]	Faricimab Q8W n = 50	Faricimab PTI n = 48	Aflibercept Q8W n = 46	Faricimab Q8W n = 580	Faricimab PTI n = 584	Aflibercept Q8W n = 579
Ocular AEs[b]	12 (24.0%)	13 (27.1%)	17 (37.0%)	223 (38.4%)	212 (36.3%)	198 (34.2%)
Serious ocular AEs[b]	0	2 (4.2%)	2 (4.3%)	15 (2.6%)	17 (2.9%)	6 (1.0%)
Ocular AEs of special interest[c]	0	2 (4.2%)	1 (2.2%)	15 (2.6%)	15 (2.6%)	5 (0.9%)
Intraocular inflammation events[d]	2 (4.0%)	1 (2.1%)	0	6 (1.0%)	8 (1.4%)	4 (0.7%)
Uveitis	1 (2.0%)	1 (2.1%)	0	1 (0.2%)	3 (0.5%)	0
Iritis	1 (2.0%)	0	0	1 (0.2%)	3 (0.5%)	2 (0.3%)
Iridocyclitis	0	0	0	2 (0.3%)	2 (0.3%)	0
Vitritis	0	0	0	3 (0.5%)	1 (0.2%)	2 (0.3%)
Anterior chamber inflammation	0	0	0	0	1 (0.2%)	0
Chorioretinitis	0	0	0	0	1 (0.2%)	0
Keratic precipitates	0	1 (2.1%)	0	0	0	0
Keratouveitis	0	0	0	0	1 (0.2%)	0
Endophthalmitis events	0	0	0	2 (0.3%)	2 (0.3%)	1 (0.2%)
Retinal vasculitis events	0	0	0	0	0	0
Retinal occlusive events						
Retinal vein occlusion	0	1 (2.1%)	0	1 (0.2%)	1 (0.2%)	0
Retinal artery occlusion	0	0	0	0	0	1 (0.2%)
Retinal artery embolism	0	0	0	0	0	1 (0.2%)
Serious non-ocular AEs	7 (14.0%)	7 (14.6%)	5 (10.9%)	120 (20.7%)	96 (16.4%)	97 (16.8%)
APTC events[e]	1 (2.0%)	0	1 (2.2%)	12 (2.1%)	12 (2.1%)	13 (2.2%)

Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population. [a]Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b]Ocular AEs in the study eye only are presented. [c] Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥ 30 letters for > 1 hour. [d]Excluding endophthalmitis. [e]APTC events were adjudicated by an external independent committee; all other events were investigator reported. Includes AEs with onset from the first dose of study drug through study end. AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; PTI, personalised treatment interval; Q8W, every 8 weeks.

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References

1. Joussen AM et al. Eye (Lond). 2021;35(5):1305-1316.
2. Wykoff C C. et al; YOSEMITE and RHINE Investigators. Lancet. 2022;399(10326):741-755.

Financial Disclosures

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- ZH, YT, HL, JRW: Employee: Genentech, Inc.
- JI: Employee: Roche Products Ltd

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

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