Faricimab Improves Fluid Parameters in Patients With Neovascular Age-Related Macular Degeneration (nAMD)

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Purpose

To evaluate fluid outcomes and the potential for extended dosing intervals with faricimab in TENAYA and LUCERNE

Conclusions

Dual Angiopoeitin-2 (Ang-2) and vascular endothelial growth factor (VEGF)-A inhibition with faricimab improved anatomical outcomes vs aflibercept during the head-to-head dosing phase, leading to extended durability

- Resolution of fluid with fewer injections with faricimab
- > 50% of faricimab-treated patients met criteria for potential every 20 weeks (Q20W) dosing intervals during the treat-and-extend (T&E) phase
- Faricimab was well tolerated, with a safety profile comparable to aflibercept

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Introduction

- Faricimab is the first bispecific antibody for intraocular use that independently binds and neutralises both Ang-2 and VEGF-A with high specificity and potency
- Year 2 data from the phase 3 TENAYA/LUCERNE (NCT03823287/NCT03823300) trials demonstrated that faricimab maintained vision with extended treatment durability and fewer injections vs aflibercept in patients with nAMD

Financial Disclosures

- RG: Consultant: AbbVie, Allergan, Bayer, Biogen, Boehringer Ingelheim, Novartis, Roche; Research: Bayer, Novartis, Roche; Advisor: Apellis
- AK: Employee: Roche Products Ltd.
- JRW, YS: Employee: Genentech, Inc.
- AS, PM: Employee: F. Hoffmann-La Roche Ltd.

Study and Product Disclosures

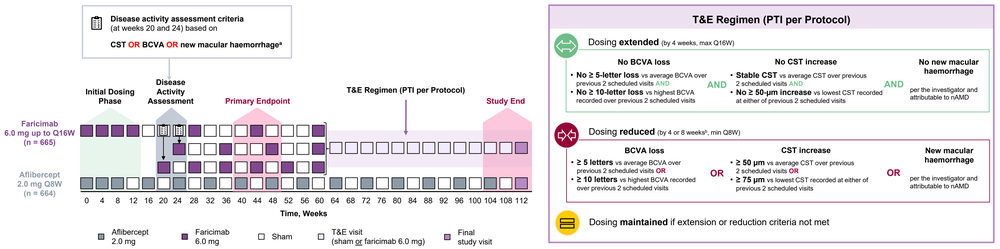
- In the UK, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema. Faricimab is not currently approved for use outside these indications in the UK
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and third-party writing assistance, which was provided by Charles Cheng, PhD, of Envision Pharma Group
- Roche conducted a factual accuracy check on the final article but any decision to incorporate comments was made solely at the discretion of the authors

References

1. Adapted from Lanzetta P et al. Presented at: American Academy of Ophthalmology Annual Meeting; September 30–October 3, 2022; Chicago, IL.

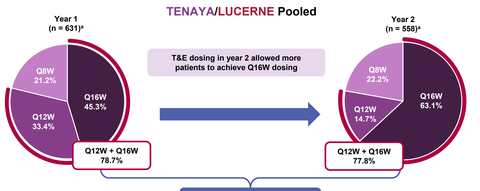
Results

1. TENAYA/LUCERNE Trials Use Disease Criteria Reflective of Clinical Practice



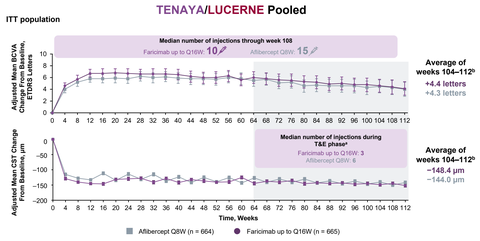
T&E regimen in TENAYA (NCT03823287) and LUCERNE (NCT03823300) uses different criteria than those used in the YOSEMITE and RHINE clinical trials. [a] Per the investigator. [b] If ≥ 2 of the reduction criteria were met or 1 criterion includes new macular haemorrhage, the interval was reduced to an 8-week interval. BCVA, best-corrected visual acuity; CST, central subfield thickness; nAMD, neovascular age-related macular degeneration; PTI, personalised treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

2. ~80% of Faricimab-Treated Patients Achieved ≥ Q12W Dosing at the End of Year 2



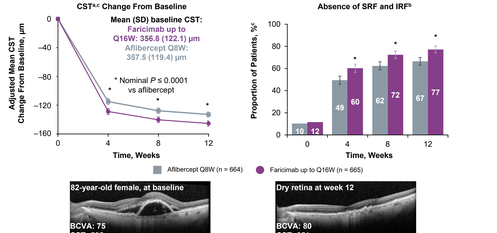
[a] Percentages are based on number of patients randomised to the faricimab arm who have not discontinued the study at that visit. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Interval at year 2 is calculated using data recorded at week 108. Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

3. Faricimab-Treated Patients Achieved Disease Control With Fewer Injections



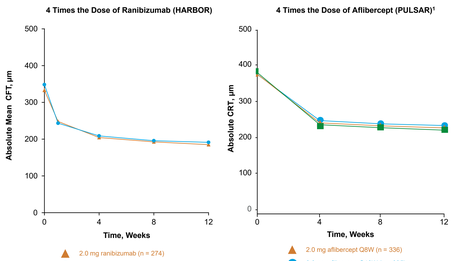
Results are based on a mixed model for repeated measures analysis in the ITT population. The median number of injections is based on the safety-evaluable population. 95% CIs are shown. CST is measured as ILM-RPE, as graded by central reading centre. [a] After week 40 to week 112: faricimab T&E phase vs aflibercept Q8W fixed dosing. Based on study design, aflibercept 2 mg was not allowed to extend beyond Q8W dosing. [b] Adjusted mean change from baseline at 2 years, averaged over weeks 104, 108 and 112. T&E dosing regimen was delayed in some patients due to dose holds or missed visits. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; T&E, treat-and-extend.

4. Anatomic Improvements With Faricimab vs Aflibercept in Head-to-Head Phase



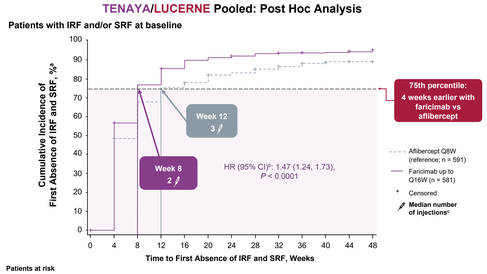
[a] CST is defined as the distance between ILM and RPE, as assessed by CRC. Results are based on a mixed model for repeated measures analysis in the ITT population. Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively. *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. [b] IRF and SRF are as measured in the central subfield (centre 1 mm). [c] All values except at baseline are weighted CMH estimates, which is based on CMH test stratified by baseline BCVA (≥ 74, 73–55, ≤ 54 letters), baseline LLD (< 33, ≥ 33 letters), region (United States and Canada vs Asia and the rest of the world) and study (TENAYA vs LUCERNE). 95% CIs are shown and estimates < 0% or > 100% are imputed as 0% or 100%, respectively. BCVA, best-corrected visual acuity; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; CRC, central reading centre; CST, central subfield thickness; ILM, internal limiting membrane; IRF, intraretinal fluid; ITT, intent-to-treat; LLD, low luminance deficient; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; SD, standard deviation; SRF, subretinal fluid.

5. Increasing Anti-VEGF Dose by 4 Times Did Not Further Improve Fluid Control



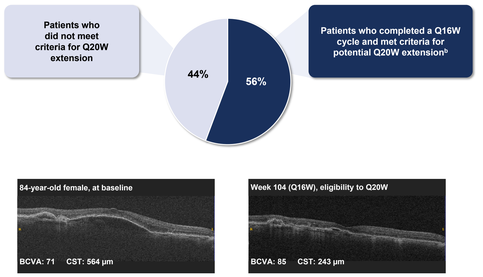
CFT, central foveal thickness; CRT, central retina thickness; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; VEGF, vascular endothelial growth factor.

6. Time to First Absence of IRF and SRF With Fewer Injections With Faricimab



Summaries of time to first absence of IRF and SRF are Kaplan–Meier estimates, with the time variable defined as the target visit week. *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. [a] Absence of retinal fluid is defined as absence of IRF and SRF. IRF and SRF are as measured in the central subfield (centre 1 mm). Event is defined as the first absence of IRF and SRF after randomisation date. Patients with absence of IRF and SRF at baseline were excluded from the analysis. [b] Results from stratified analyses are presented for HR and log-rank test. Stratification factors are baseline BCVA (≥ 74, 73–55, ≤ 54 letters), baseline LLD (< 33, ≥ 33 letters), region (United States and Canada, Asia and the rest of the world) and study (TENAYA vs LUCERNE). HRs were estimated by Cox regression. An HR > 1 favours faricimab over aflibercept. [c] The number of injections includes any active drug administered (faricimab or aflibercept), including medication errors. BCVA, best-corrected visual acuity; CI, confidence interval; HR, hazard ratio; IRF, intraretinal fluid; LLD, low-luminance deficit; Q8W, every 8 weeks; Q16W, every 16 weeks; SRF, subretinal fluid.

7. > 50% of Faricimab-Treated Patients Met Criteria for Potential Q20W Dosing



[a] Limited to subjects who had ≥ 1 faricimab dose during the T&E phase. [b] The same protocol defined extension criteria for personalised T&E was used in this analysis. BCVA, best-corrected visual acuity; CST, central subfield thickness; Q16W, every 16 weeks; Q20W, every 20 weeks; T&E, treat-and-extend.

8. Faricimab Was Well Tolerated With a Safety Profile Comparable to Aflibercept

AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	TENAYA/LUCERNE Pooled: Faricimab Up to Q16W n = 664	TENAYA/LUCERNE Pooled: Aflibercept Q8W n = 662
Ocular AEs[b]	358 (53.9)	345 (52.1)
Serious ocular AEs[b]	29 (4.4)	29 (4.4)
Ocular AEs of special interest[c]	25 (3.8)	27 (4.1)
Intraocular inflammation events[d]	20 (3.0)	15 (2.3)
Uveitis	4 (0.6)	3 (0.5)
Iritis	8 (1.2)	3 (0.5)
Iridocyclitis	2 (0.3)	1 (0.2)
Vitritis	4 (0.6)	1 (0.2)
Post-procedural inflammation	0	5 (0.8)
Chorioretinitis	1 (0.2)	0
Keratic precipitates	2 (0.3)	0
Non-infectious endophthalmitis	0	1 (0.2)
Anterior chamber flare	0	1 (0.2)
Endophthalmitis events	3 (0.5)	2 (0.3)
Retinal vasculitis events	0	0
Retinal occlusive events		
Retinal vein occlusion	0	0
Retinal artery occlusion	0	0
Retinal artery embolism	1 (0.2)[f]	0
Serious nonocular AEs	138 (20.8)	162 (24.5)
APTC events[e]	22 (3.3)	20 (3.0)

[a] Results are presented for the pooled safety-evaluable populations. 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. [f] Hollenhorst plaque that was reported at the end of year 1 and was not treatment related as per the investigator. AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; Q8W, every 8 weeks; Q16W, every 16 weeks.