Efficacy, Safety and Durability of Faricimab in nAMD: Year 2 Results From the Phase 3 TENAYA and LUCERNE Trials

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On behalf of the TENAYA and LUCERNE Investigators

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Key Clinical Question

To present the results of the year 2 data from the TENAYA and LUCERNE pivotal trials and to evaluate the impact of faricimab on fluid outcomes

Introduction

- Faricimab is the first bispecific antibody for intraocular use that independently binds and neutralises both angiopoietin-2 and vascular endothelial growth factor-A with high specificity and potency
- TENAYA/LUCERNE (NCT03823287/NCT03823300) were randomised, active comparator–controlled, 112-week trials that evaluated the efficacy, durability and safety of faricimab compared with aflibercept in patients with neovascular age-related macular degeneration (nAMD)
- Year 1 data from TENAYA/LUCERNE suggest that faricimab promotes vascular stability/durable efficacy in patients with nAMD[1]
- Year 2 of TENAYA/LUCERNE evaluated the longer-term efficacy, durability and safety of faricimab in patients with nAMD

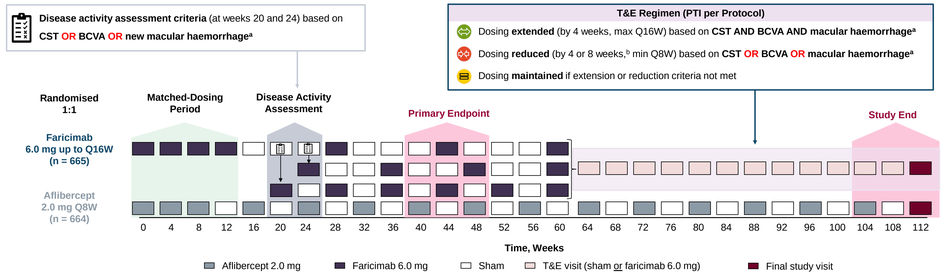
Methods

- Patients with nAMD were randomized 1:1 to either faricimab up to Q16W (n=665) or aflibercept Q8W (n=664)
- Aflibercept-treated patients received 3 initial Q4W doses and then Q8W dosing. After 4 initial doses Q4W, faricimab-treated patients were treated Q8W, Q12W, or Q16W based on protocol-defined disease activity assessments at weeks 20 or 24.
- At week 60, all faricimab-treated patients had an injection and entered the protocol-driven treat-and-extend–based personalized treatment interval (PTI) regimen where dosing intervals could be extended by 4 weeks (up to Q16W), maintained or reduced by 4 or 8 weeks (as low as Q8W), based on CST and BCVA change at active dosing visits.
- The primary endpoint was mean change from baseline in best-corrected visual acuity (BCVA) averaged over weeks 40, 44, and 48. Secondary endpoints, including visual and anatomical outcomes and safety were assessed Q4W through to week 112. The final visit was at week 112.

Conclusions

- Durable vision gains and anatomic outcomes with faricimab were achieved at the end of the first year and maintained at year 2, with ~80% of patients with ≥ every-12-weeks dosing
- Faricimab led to greater drying on optical coherence tomography (OCT) during the matched-dosing period and faster drying on OCT versus aflibercept with fewer injections
- Faricimab was well tolerated, with a safety profile comparable with aflibercept
- The ongoing AVONELLE-X long-term extension study will generate 4-year data
- At 112 weeks patients were rolled into the ongoing long-term extension study AVONELLE-X where all patients will be administered faricimab according to the T&E based PTI dosing regimen for the duration of the study

TENAYA and LUCERNE Trial Design: Faricimab nAMD Trials Use Disease Criteria Reflective of Clinical Practice



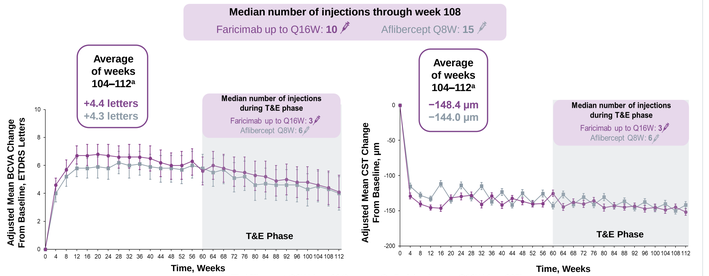
Patients whose treatment interval is reduced by 8 weeks from Q16W to Q8W will not be allowed to return to a Q16W interval during the study
[a] Per the investigator. b If ≥ 2 of the reduction criteria were met or 1 criterion includes new macular haemorrhage, the interval was reduced to an 8-week interval.
BCVA, best-corrected visual acuity; CST, central subfield thickness; max, maximum; min, minimum; nAMD, neovascular age-related macular degeneration; PTI, personalised treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

Results 1: Key Baseline Characteristics Were Generally Well Balanced Across Treatment Arms

	TENAYA/LUCERNE Pooled	
Characteristic	Faricimab Up to Q16W n = 665	Aflibercept Q8W n = 664
Age, years, mean (SD)[a]	75.4 (8.5)	76.4 (8.7)
Sex, female, n (%)	394 (59.2%)	399 (60.1%)
Race, White, n (%)[b]	581 (87.4%)	572 (86.1%)
BCVA, ETDRS letters, mean (SD)	60.0 (13.3)	60.2 (13.1)
CST, µm, mean (SD)[c]	356.8 (122.1)	357.5 (119.4)
Phakic, n (%)	383 (57.6%)	369 (55.6%)
Presence of IRF, n (%)	288 (43.3%)	311 (46.8%)
Presence of SRF, n (%)	437 (65.7%)	447 (67.3%)
CNV location by FFA, n (%)		
Subfoveal	410 (61.7%)	377 (56.8%)
Juxtafoveal	161 (24.2%)	172 (25.9%)
Extrafoveal	83 (12.5%)	99 (14.9%)

Results are presented for the pooled TENAYA/LUCERNE ITT population. a Age is at randomisation. b Not all race categories are presented; percentages do not add up to 100. c CST is measured as ILM-RPE. BCVA, best-corrected visual acuity; CNV, choroidal neovascularisation; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; FFA, fundus fluorescein angiography; ILM, internal limiting membrane; IRF, intraretinal fluid; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; SRF, subretinal fluid.

Results 2: Over 2 Years, Patients in the Faricimab Arm Achieved Disease Control With Fewer Injections



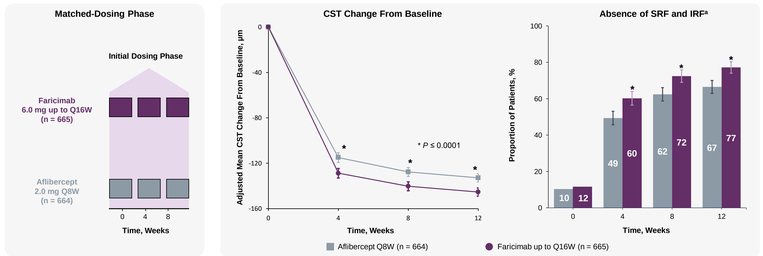
Results are based on a mixed model for repeated measures analysis in the ITT population. The median number of injections is based on the safety-evaluable population. 95% CIs are shown. CST is measured as ILM-RPE, as graded by central reading centre. a Adjusted mean change from baseline at 2 years, averaged over weeks 104, 108 and 112. PTI dosing regimen was delayed in some patients due to dose holds or missed visits. BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; ITT, intent-to-treat; Q8W, every 8 weeks; PTI, personalised treatment interval; Q16W, every 16 weeks; RPE, retinal pigment epithelium; T&E, treat-and-extend.

Safety: Faricimab Was Well Tolerated, With a Safety Profile Comparable With Aflibercept Through Year 2

	TENAYA/LUCERNE Pooled	
AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	Faricimab Up to Q16W n = 664	Aflibercept Q8W n = 662
Ocular AEs[b]	358 (53.9%)	345 (52.1%)
Serious non-ocular AEs[b]	29 (4.4%)	29 (4.4%)
Ocular AEs of special interest[b,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%)[e]	0
Serious non-ocular Aes	138 (20.8%)	162 (24.5%)
APTC events[f]	22 (3.3%)	20 (3.0%)

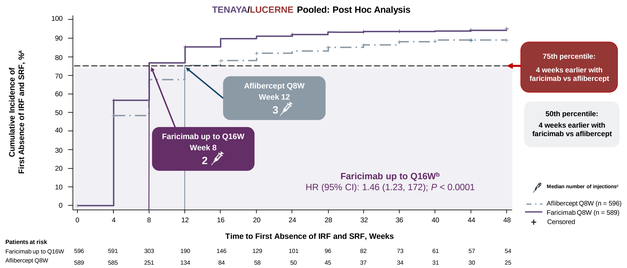
[a] Results are presented for the pooled TENAYA/LUCERNE safety-evaluable populations. Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b]Ocular AEs in the study eye only are presented. [c]Ocular AEs of special interest 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 Hollenhorst plaque that was reported at the end of year 1 and was not treatment related as per the investigator. f APTC events were adjudicated by an external independent committee; all other events were investigator reported.
AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; Q8W, every 8 weeks; Q16W, every 16 weeks.

Results 3: Greater Anatomic Improvements With Faricimab vs Aflibercept During the Matched-Dosing Period



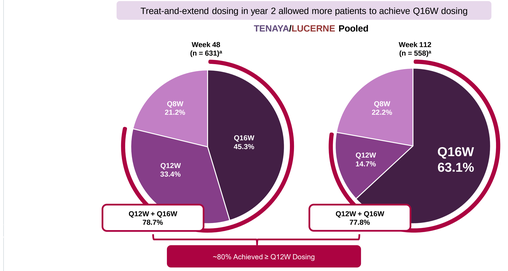
Results are based on a mixed model for repeated measures analysis in the ITT population. Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively. CST is measured as ILM-RPE, as graded by a central reading centre. P values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the P values. Clinical significance has not been established and conclusions regarding treatment effect cannot be drawn. a IRF and SRF are as measured in the central subfield (centre 1 mm). 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 the rest of the world) and study (GR40306 vs GR40844). 95% CIs are shown and estimates < 0% or > 100% are imputed as 0% or 100%, respectively. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; ILM, internal limiting membrane; IRF, intraretinal fluid; ITT, intent-to-treat; LLD, low-luminance deficit; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; SRF, subretinal fluid.

Results 4: Faricimab-Treated Patients Achieved First Absence of IRF and SRF Faster and With Fewer Injections vs Aflibercept



Results are presented for the pooled TENAYA/LUCERNE ITT population (patients with IRF and SRF at baseline). 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. Clinical significance has not been established and conclusions regarding treatment effect cannot be drawn. 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 (GR40306 vs GR40844). 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; HR, hazard ratio; IRF, intraretinal fluid; ITT, intent-to-treat; LLD, low-luminance deficit; Q8W, every 8 weeks; Q16W, every 16 weeks; SRF, subretinal fluid.

Results 5: ~80% of Faricimab-Treated Patients Achieved ≥ Q12W Dosing at 2 Years



Results are presented for the pooled TENAYA/LUCERNE ITT population. 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 week 112 is calculated using data recorded at week 108. b Weeks 60–112.
ITT, intent-to-treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

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References
1. Khanani AM et al. Ophthalmol Sci. 2021;1(4):10076.

Financial Disclosures
- PP: Consultant: Roche, Genentech, Novartis, Bayer, BI.
- DS: Employee: Roche Products Ltd
- BS: Employee: F. Hoffmann-La Roche Ltd.
- VP, AK: Employee: Roche Products Ltd.
- HL, JRW: Employee: Genentech, Inc.

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
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and writing assistance, which was provided by Saima Khokhar, Medical Affairs Partner of Roche Products Ltd, UK