Faricimab in Neovascular Age-Related Macular Degeneration: 1-Year Efficacy, Safety and Durability in the Phase 3 TENAYA and LUCERNE Trials

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Key Clinical Question

What is the efficacy, safety and durability of faricimab, a dual angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) inhibitor, in patients with neovascular age-related macular degeneration (nAMD)?

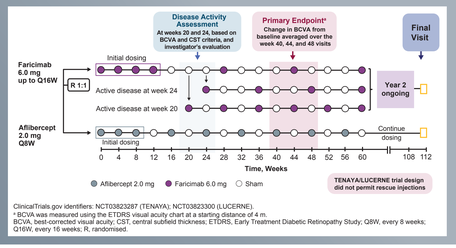
Introduction

- Upregulation of both Ang-2 and VEGF-A are key drivers of vascular destabilisation in nAMD and other retinal vascular diseases[1-3]
- Dual inhibition of Ang-2 and VEGF-A with faricimab, the first bispecific antibody designed for intraocular use, may promote vascular stability with treatment benefits over conventional anti-VEGF monotherapy for nAMD[4,5]

Methods

- TENAYA (NCT03823287) and LUCERNE (NCT03823300) are identical, phase 3, randomised, double-masked, comparator-controlled, 112-week studies of patients with nAMD
- TENAYA and LUCERNE enrolled 1329 patients across 271 sites worldwide, including 15 UK sites
- Treatment-naïve patients were randomised 1:1 to faricimab 6.0 mg up to every 16 weeks (Q16W) or aflibercept 2.0 mg up to every 8 weeks (Q8W)
- Primary efficacy endpoint: mean change in best-corrected visual acuity (BCVA) from baseline averaged over weeks 40, 44 and 48
- Secondary endpoints: proportion of patients receiving faricimab Q16W, every 12 weeks (Q12W) and Q8W; and optical coherence tomography (OCT)[a] changes
- Safety outcomes included incidence and severity of ocular and non-ocular adverse events

[a] OCT was measured by spectral-domain or certain permitted swept-source OCT devices by certified site personnel.



ClinicalTrials.gov identifiers: NCT03823287 (TENAYA); NCT03823300 (LUCERNE).
[a] BCVA was measured using the ETDRS visual acuity chart at a starting distance of 4 m.
BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Q8W, every 8 weeks; Q16W, every 16 weeks; R, randomised.

Conclusions

- TENAYA and LUCERNE met the primary endpoint of non-inferiority in mean change from baseline in BCVA with faricimab dosed up to Q16W compared with aflibercept Q8W in patients with nAMD at week 48[a]
- Faricimab demonstrated disease control based on durability up to Q16W at week 48 and meaningful reductions in central subfield thickness with faricimab up to Q16W comparable with aflibercept Q8W through week 48
- Faricimab was well tolerated and no cases of vasculitis or occlusive retinitis were reported
- TENAYA and LUCERNE are 2-year studies. The long-term extension study, AVONELLE-X, will generate 4-year long-term data

[a] Primary endpoint was averaged over weeks 40, 44 and 48.

1. Key Baseline Ocular Characteristics Were Generally Well Balanced Across Treatment Arms

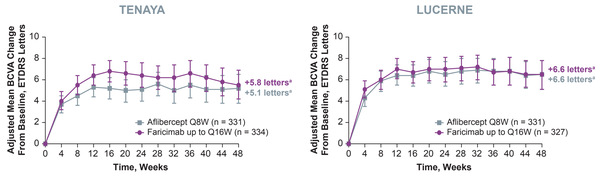
ITT Population

	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 334)	Aflibercept Q8W (n = 337)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 327)
Age, years, mean (SD)	75.9 (8.6)	76.7 (8.8)	74.8 (8.4)	76.1 (8.6)
Sex, n (%): Female	191 (57.2%)	211 (62.6%)	203 (61.3%)	188 (57.5%)
Race, n (%)[a]: White	303 (90.7%)	302 (89.6%)	278 (84.0%)	270 (82.6%)
BCVA, ETDRS letters, mean (SD)	61.3 (12.5)	61.5 (12.9)	58.7 (14.0)	58.9 (13.3)
CST,[b] µm, mean (SD)	360.5 (124.1)	356.1 (107.0)	353.1 (120.1)	359.0 (131.1)
Phakic, n (%)	193 (57.8%)	184 (54.6%)	190 (57.4%)	185 (56.6%)
Presence of IRF, n (%)	146 (43.7%)	157 (46.6%)	142 (42.9%)	154 (47.1%)
Presence of SRF, n (%)	216 (64.7%)	225 (66.8%)	221 (66.8%)	222 (67.9%)
CNV location by FFA, n (%):				
Subfoveal	201 (60.2%)	186 (55.2%)	209 (63.1%)	191 (58.4%)
Juxtafoveal	88 (26.3%)	88 (26.1%)	73 (22.1%)	84 (25.7%)
Extrafoveal	41 (12.3%)	55 (16.3%)	42 (12.7%)	44 (13.5%)

[a] Not all race categories are presented; percentages do not add up to 100. Age is at randomisation. [b] 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.

2. Primary Endpoint Met: BCVA Gains From Baseline With Faricimab Dosed up to Q16W Were Non-inferior to Aflibercept Q8W

ITT Population



Faricimab up to Q16W vs aflibercept Q8W averaged over weeks 40, 44 and 48[a] (ETDRS letters), mean (95.03% CI)
+0.7 (−1.1, +2.5)

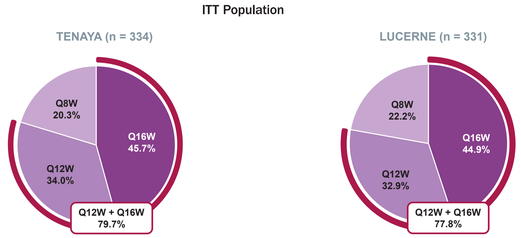
Faricimab up to Q16W vs aflibercept Q8W averaged over weeks 40, 44 and 48[a] (ETDRS letters), mean (95.03% CI)
0.0 (−1.7, +1.8)

Results are based on a mixed model for repeated measures analysis in the ITT population. 95.03% CIs are shown.
[a] Adjusted mean BCVA change from baseline at 1 year, averaged over weeks 40, 44 and 48.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks.

3. Durability With Faricimab: ~45% of Patients on Q16W and Almost 80% on ≥ Q12W Dosing at Week 48

- Proportion of patients in the faricimab arm on each treatment interval among those completing week 48

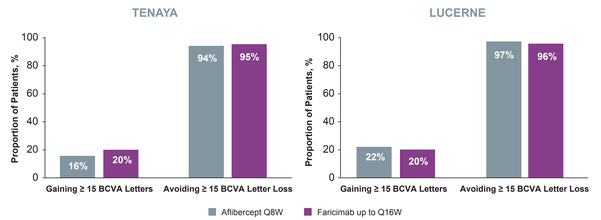
ITT Population



Median number of injections: faricimab: 6; aflibercept: 8 (data source: safety-evaluable population). Percentages are based on number of patients randomised to the faricimab arm who have not discontinued the study at week 48. Treatment interval at week 48 is defined as the treatment interval decision followed at that visit.
ITT, intent-to-treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

4. Comparable Proportion of Patients Gaining or Maintaining Vision[a] With Faricimab up to Q16W and Aflibercept Q8W

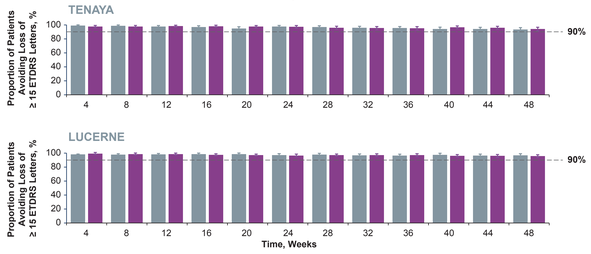
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Includes patients with ≥ 1 non-missing assessment at weeks 40, 44 and 48 (TENAYA: aflibercept, n = 300; faricimab, n = 292; LUCERNE: aflibercept, n = 291; faricimab, n = 302).
Proportion of patients in each group was estimated using the CMH method (95.03% CI).
[a] Proportion of patients who gained or avoided a loss of ≥ 15 ETDRS letters at 1 year, averaged over weeks 40, 44 and 48.
BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks.

5. Consistently High and Comparable Proportion of Patients With Stable Vision[a] Across Treatment Arms in Both Studies

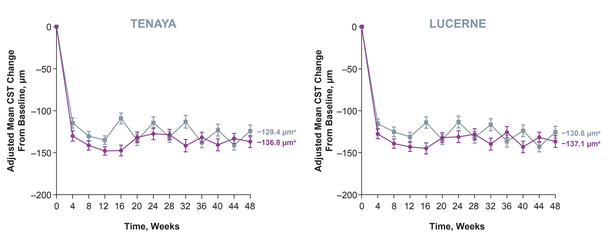
ITT Population



Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively. Missing data were not imputed.
[a] Proportion of patients who avoided a loss of ≥ 15 ETDRS letters. Proportion of patients in each group was estimated using the CMH method. 95.03% CIs are shown.
CMH, Cochran-Mantel-Haenszel; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks.

6. Meaningful and Comparable Reductions in CST From Baseline Through Week 48 With Faricimab up to Q16W and Aflibercept Q8W

ITT Population



Results are based on a mixed model for repeated measures analysis. 95.03% CIs are shown. CST is measured as ILM-RPE, as graded by central reading centre.
[a] Adjusted mean CST change from baseline at 1 year, averaged over weeks 40, 44 and 48.
CST, central subfield thickness; ILM, internal limiting membrane; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium.

7. Low Rates of AEs

	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Total number of AEs[a]	858	812	812	846
Total number of SAEs[a]	47	67	68	122
Total number of deaths, n (%)	5 (1.5%)	1 (0.3%)	4 (1.2%)	7 (2.1%)
Patients with any ocular AE, n (%)[b]	121 (36.3%)	128 (38.1%)	133 (40.2%)	118 (36.2%)
Patients with any ocular SAE, n (%)[b]	4 (1.2%)	6 (1.8%)	7 (2.1%)	7 (2.1%)
Patients with any non-ocular SAE, n (%)	30 (9.0%)	34 (10.1%)	38 (11.5%)	48 (14.7%)
Patients with any treatment-related ocular AE, n (%)[b]	9 (2.7%)	9 (2.7%)	10 (3.0%)	8 (2.5%)
Patients with any treatment-related ocular SAE, n (%)[b]	3 (0.9%)	0	5 (1.5%)	1 (0.3%)
Patients with any AE of special interest, n (%)[c]	3 (0.9%)	12 (3.6%)	11 (3.3%)	8 (2.5%)
Patients with any APTC[c] events, n (%)	3 (0.9%)	3 (0.9%)	4 (1.2%)	3 (0.9%)

Results are presented based on the safety-evaluable population. All safety are investigator reported.
[a] Total number of AEs and SAEs includes non-ocular and ocular events in the study or fellow eye. [b] Ocular AEs and SAEs in the study eye only are presented in all safety outputs. [c] AEs of special interest include events associated with severe intraocular inflammation that result in a BCVA drop of > 30 letters for > 1 hour, or those that require intervention/surgery to prevent permanent vision loss. Percentages are based on n in the column headings. Multiple occurrences of the same AE in an individual are counted only once, except for the "Total number of AEs" and "Total number of SAEs" rows, in which multiple occurrences of the same AE are counted separately. Includes AEs with onset up to day 349 (last day of week 48 analysis visit window).
[d] APTC events were adjudicated by an external committee.
AE, adverse event; APTC, Anti-Platelet Trialists' Collaboration; Q8W, every 8 weeks; Q16W, every 16 weeks; SAE, serious adverse event.

8. Low Rates of Ocular AEs

- IOI events were on average reported in 2.0% and 1.2% of patients for faricimab and aflibercept, respectively
- No cases of retinal vasculitis reported in either study
- A single asymptomatic retinal artery embolism (a Hollenhorst plaque) was reported by the investigator in the faricimab arm of LUCERNE

	TENAYA		LUCERNE	
IOI Through Week 48	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Patients with any AEs of IOI (excluding endophthalmitis), n (%)	5 (1.5%)	2 (0.6%)	8 (2.4%)	6 (1.8%)
Patients with events, n (%)				
Iritis	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (0.3%)
Uveitis	1 (0.3%) **S**	1 (0.3%)	1 (0.3%) **S**	1 (0.3%) **S**
Keratic precipitates	1 (0.3%)	0	0	0
Vitritis	1 (0.3%)	0	2 (0.6%)	1 (0.3%)
Iridocyclitis	0	0	3 (0.9%)	2 (0.6%)
Chorioretinitis	0	0	1 (0.3%) **S**	0
Postprocedural inflammation	0	0	0	1 (0.3%)

	TENAYA		LUCERNE	
IOI Through Week 48	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Endophthalmitis, n (%)	0	0	0	1 (0.3%)

Results are presented based on the safety-evaluable population. All events are investigator reported. For frequency counts by Preferred Term, multiple occurrences of the same AE in an individual are counted only once. Includes AEs with onset up to day 349 (last day of week 48 analysis visit window). S: severe events are called out; all other events were mild or moderate.
AE, adverse event; IOI, intraocular inflammation; Q8W, every 8 weeks; Q16W, every 16 weeks.

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Financial Disclosures

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- CQR, HL: Employee: Genentech, Inc.
- DS, JI: Employee: Roche Products Ltd.
- KB: Employee: Roche Products (Ireland) Ltd.

Study Disclosures

- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation

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