Faricimab in Neovascular Age-Related Macular Degeneration: 48-Week Results by Dosing Cohort in the TENAYA/LUCERNE Trials Exploratory Analysis

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On behalf of the TENAYA and LUCERNE Investigators

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Key Clinical Question

What is the impact of different dosing intervals on treatment outcomes in TENAYA and LUCERNE?

Introduction

- Faricimab is the first bispecific antibody for intraocular use that independently binds and neutralizes both angiopoietin-2 and VEGF-A with high specificity and potency[1]
- 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[2]
- We present efficacy data on the different faricimab dosing cohorts in TENAYA and LUCERNE and these are exploratory analysis and not type 1 error controlled

Methods

- Patients with nAMD were randomized 1:1 to either the faricimab up to Q16W (n=665) or aflibercept Q8W arm (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 and 24
- Patients with active disease at week 20 received Q8W dosing, patients with active disease only at week 24 received Q12W dosing, patients with no evidence of active disease at weeks 20 and 24 received Q16W dosing
- The primary endpoint was change from baseline in BCVA averaged over weeks 40, 44, and 48 and the final visit was at week 112[3]

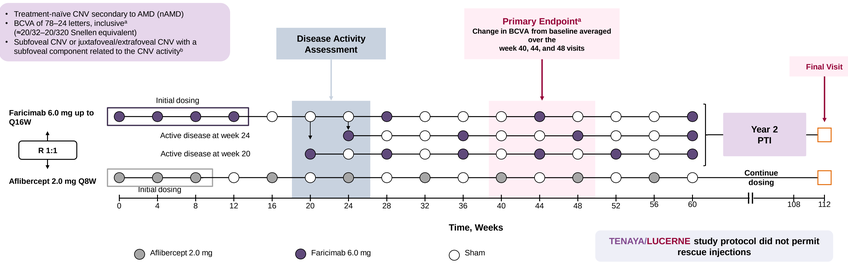
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Conclusions

- All faricimab cohorts showed sustained vision gains and decreases in central subfield thickness during the maintenance phase that were similar between cohorts.
- ~45% of patients on the Q16W dosing interval exhibited early vision gains and central subfield thickness reductions that were stable throughout the maintenance phase despite receiving only two faricimab injections. ~33% of patients in the faricimab Q12W treatment interval also achieved comparable early vision gains that were generally sustained throughout the maintenance phase. In the ~21% of patients who required Q8W dosing during the maintenance phase, vision outcomes were comparable to the other two faricimab treatment intervals.
- Regardless of treatment interval, the rapid vision gains and reduction in CST from the initiation phase were maintained through the first year with nearly 80% of patients in the faricimab extending dosing cohort receiving only 2-3 injections during the maintenance phase until week 48.
- Increased BCVA and CST variability observed for shorter treatment intervals reflects the small subgroup size and the findings should be interpreted with caution.

1. TENAYA and LUCERNE investigated Faricimab Using an Individualized Treatment Interval of Up to Q16W Dosing

- Treatment-naïve CNV secondary to AMD (nAMD)
- BCVA of 78–24 letters, inclusive[a]
- (+20/32–20/320 Snellen equivalent)
- Subfoveal CNV or juxtafoveal/extrafoveal CNV with a subfoveal component related to the CNV activity[b]

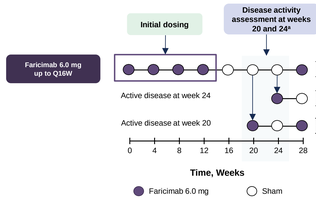


[a] BCVA was measured using the ETDRS visual acuity chart at a starting distance of 4 m. [b] Identified by FFA or OCT.AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; ETDRS, Early Treatment Diabetic Retinopathy Study; FFA, fundus fluorescein angiography; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; R, randomized.

2.Following Initial Dosing and Disease Activity Assessments, Patients in the Faricimab Arm Were Treated With Fixed Q16W, Q12W, or Q8W Intervals

Faricimab Arm

- Initial Q4W dosing consistent with STAIRWAY[4]
- Administered Q8W–Q16W after initial dosing **until week 60**; treatment intervals informed by the phase 2 STAIRWAY[1] trial



Disease Activity Criteria (Active Disease if *Any* Are Met)

OCT

- Increase in CST > 50 µm compared with average CST over previous 2 scheduled visits[b]
- Increase in CST ≥ 75 µm compared with lowest CST recorded at either of previous 2 scheduled visits[b]

OR

Visual Acuity

- Decrease of ≥ 5 letters of BCVA compared with average BCVA over previous 2 scheduled visits, due to nAMD (per the investigator)
- Decrease of ≥ 10 letters of BCVA compared with highest BCVA recorded over previous 2 scheduled visits, due to nAMD (per the investigator)

OR

Clinical Examination

- Presence of new macular hemorrhage (per the investigator), due to nAMD activity
- Investigator opinion of significant nAMD disease activity at week 24 that requires immediate treatment **(applies only at week 24)**

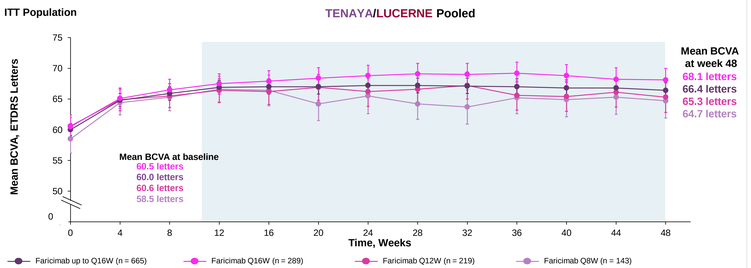
[a] Two disease activity assessments allow investigators to identify those patients for whom an extended dosing interval is not suitable. [b] CST values obtained at site were entered into the IxRS at weeks 12, 16, 20, and 24, for the determination of disease activity.
BCVA, best-corrected visual acuity; CST, central subfield thickness; IxRS, interactive voice or web-based response system; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

3.Patients Who Required Faricimab Q8W Dosing Generally Had Worse Baseline Ocular Characteristics vs Extended Treatment Intervals

		TENAYA/LUCERNE Pooled		
		Faricimab Q8W (n = 143)	Faricimab Q12W (n = 219)	Faricimab Q16W (n = 289)
BCVA, ETDRS letters, mean (SD)		58.5 (14.1)	60.6 (13.4)	60.5 (12.6)
BCVA categories, n (%):	≥ 74 (20/32 or better)	16 (11.2%)	35 (16.0%)	41 (14.2%)
	73–55 (20/40–20/80)	74 (51.7%)	119 (54.3%)	178 (61.6%)
	≤ 54 (20/80 or worse)	53 (37.1%)	65 (29.7%)	70 (24.2%)
LLD, ETDRS letters, mean (SD)		27.0 (12.6)	25.0 (12.5)	24.3 (13.0)
CST, µm, mean (SD)[a]		383.2 (141.6)	353.9 (123.2)	346.5 (109.4)
Presence of IRF, n (%)		60 (42.0%)	87 (39.7%)	131 (45.3%)
Presence of SRF, n (%)		91 (63.6%)	140 (63.9%)	199 (68.9%)
Total area of CNV lesions by FFA, mm², mean (SD)		5.8 (5.2)	5.0 (5.0)	3.9 (4.2)
CNV location by FFA, n (%)[b]:	Subfoveal	106 (74.1%)	143 (65.3%)	153 (52.9%)
	Juxtafoveal	24 (16.8%)	51 (23.3%)	83 (28.7%)
	Extrafoveal	10 (7.0%)	22 (10.0%)	48 (16.6%)
CNV lesion type by FFA, n (%)[b]:	Occult	85 (59.4%)	116 (53.0%)	142 (49.1%)
	Classic	36 (25.2%)	62 (28.3%)	80 (27.7%)
	Minimally classic	13 (9.1%)	21 (9.6%)	25 (8.7%)
	RAP	2 (1.4%)	6 (2.7%)	19 (6.6%)

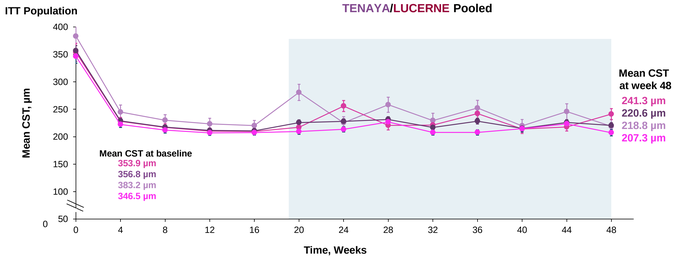
[a] CST is measured as ILM-RPE. [b] Not all categories are presented; percentages do not add up to 100.
. BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; FFA, fundus fluorescein angiography; ILM, internal limiting membrane; IRF, intraretinal fluid; ITT, intent-to-treat; LLD, low-luminance deficit; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; RAP, retinal angiomatous proliferation; RPE, retinal pigment epithelium; SRF, subretinal fluid.

4.Meaningful Visual Improvements Were Achieved and Maintained Through Week 48, Regardless of Faricimab Treatment Interval



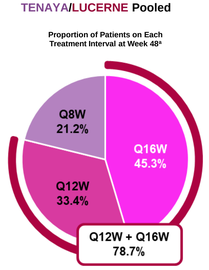
95% CIs are shown. Results are based on descriptive summary.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent-to-treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

5.Meaningful Anatomical Improvements Were Achieved and Maintained Through Week 48, Regardless of Faricimab Treatment Interval



95% CIs are shown. CST is defined as the distance between ILM and RPE, as assessed by central reading center. Results are based on descriptive summary.
CST, central subfield thickness; ILM, internal limiting membrane; ITT, intent-to-treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium.

6. Proportion of patients on each treatment interval at week 48



[a] Percentages are based on number of patients randomized 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. Treatment intervals are not determined for patients randomized to Faricimab who discontinued study prior to disease activity assessments visits.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent-to-treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

7. Faricimab Was Well Tolerated Through Study End

	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 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%)[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.

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References

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Financial Disclosures

- JT: Advisory Board/Research Grant: Roche, Bayer, Novartis, Allmera.
- CQ, HL, JRW: Employees: Genentech, Inc..
- JI, AK: Employee: Roche Products Ltd.
- BS: Employee: F. Hoffmann-La Roche 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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