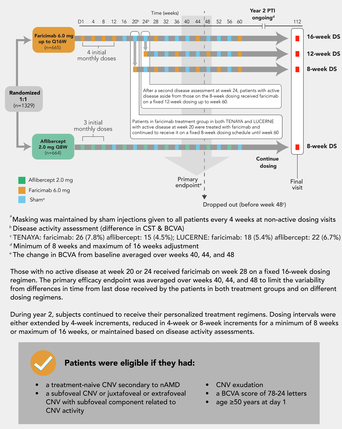
Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): Two randomized, double-masked, phase 3, non-inferiority trials

Heier JS, Khanani AM, Quezada Ruiz C, et al. *Lancet*. 2022;399:729-740.
doi:10.1016/S0140-6736(22)00010-1

Real-world patient outcomes of treatment of neovascular age-related macular degeneration (nAMD) with intravitreal anti-vascular endothelial growth factor (VEGF) therapy tend to be suboptimal because of the treatment burden associated with frequent monitoring and injection visits. Additionally, novel targets beyond the VEGF pathway may be implicated in the pathogenesis of nAMD and can be targeted for improved patient outcomes. The upregulation of angiopoietin-2 (Ang-2) in nAMD indirectly results in vascular leakage and negatively regulates the Ang-Tie pathway, which plays a key role in vascular homeostasis and regulation. Therefore, dual Ang-2 and VEGF-A inhibition may synergistically promote vascular stability and may be a more effective strategy for treatment than anti-VEGF therapy alone. Previous studies examining dual inhibition of both pathways has demonstrated the potential for reduced vascular leakage and inflammation than with VEGF-A inhibition alone.

Ang-Tie = angiopoietin-tyrosine kinase with immunoglobulin-like and epidermal growth factor homology domains

TENAYA and LUCERNE were identical, randomized, double-masked, multicenter, phase 3 trials designed to evaluate the efficacy, safety, and durability of faricimab compared with aflibercept.



*Masking was maintained by sham injections given to all patients every 4 weeks at non-active dosing visits
†Disease activity assessment (difference in CST & BCVA)
‡TENAYA: faricimab: 26 (7.8%) aflibercept: 15 (4.5%); LUCERNE: faricimab: 18 (5.4%) aflibercept: 22 (6.7%)
§Minimum of 8 weeks and maximum of 16 weeks adjustment
¶The change in BCVA from baseline averaged over weeks 40, 44, and 48

Those with no active disease at week 20 or 24 received faricimab on week 28 on a fixed 16-week dosing regimen. The primary efficacy endpoint was averaged over weeks 40, 44, and 48 to limit the variability from differences in time from last dose received by the patients in both treatment groups and on different dosing regimens.

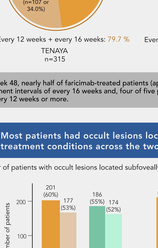
During year 2, subjects continued to receive their personalized treatment regimens. Dosing intervals were either extended by 4-week increments, reduced in 4-week or 8-week increments for a minimum of 8 weeks or maximum of 16 weeks, or maintained based on disease activity assessments.

Patients were eligible if they had:

- a treatment-naive CNV secondary to nAMD
- a subfoveal CNV or juxtafoveal or extrafoveal CNV with subfoveal component related to CNV activity
- CNV exudation
- a BCVA score of 78-24 letters
- age ≥50 years at day 1

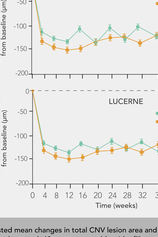
CST = central subfield thickness; CNV = choroidal neovascularization; BCVA = best-corrected visual acuity

Approximately 80% of patients treated with faricimab in both TENAYA and LUCERNE stayed on extended fixed treatment of every 12 or 16 weeks, demonstrating the sustained efficacy of faricimab.

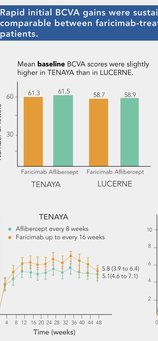


At week 48, nearly half of faricimab-treated patients (approximately 45%) were on extended fixed treatment intervals of every 16 weeks and, four of five patients (approximately 80%) on intervals of every 12 weeks or more.

Most patients had occult lesions located subfoveally in the two treatment conditions across the two trials.

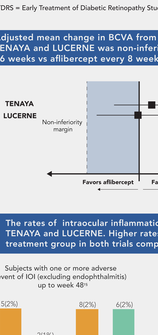


In both TENAYA and LUCERNE, anatomical outcomes using spectral domain optical coherence tomography (SD-OCT) supported functional outcomes.



Adjusted mean changes in total CNV lesion area and total area of leakage from baseline with faricimab at week 48 were comparable with aflibercept. Additionally, patient-reported vision-related functioning and quality of life was also comparable between treatment groups.

Rapid initial BCVA gains were sustained up to week 48 and were comparable between faricimab-treated and aflibercept-treated patients.



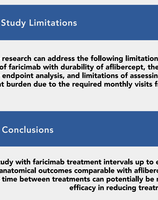
Most patients in TENAYA and LUCERNE had a baseline BCVA score of 73-55 letters (Snellen equivalent 20/40-20/80) and patients in both trials gained 10 or more OR 15 or more EDTRS letters at the primary endpoint visits.

These BCVA gains were sustained up to week 48 and 95% of patients across treatment groups in both trials avoided the loss of 15 letters or more.

The difference in adjusted mean BCVA change for TENAYA (0.7) for the two treatments favored faricimab and the lower bounds of the two-sided 95% CIs for difference in adjusted means of both treatments were within the non-inferiority margin of 4 letters therefore establishing inferiority of faricimab to aflibercept.

ETDRS = Early Treatment of Diabetic Retinopathy Study; CI = confidence interval

Adjusted mean change in BCVA from baseline up to week 48 in TENAYA and LUCERNE was non-inferior with faricimab up to every 16 weeks vs aflibercept every 8 weeks.



The rates of intraocular inflammation (IOI) were low across both TENAYA and LUCERNE. Higher rates were reported in the faricimab treatment group in both trials compared with aflibercept in both trials.

† Ocular adverse events and serious adverse events in the study eye only
§ Includes serious and non-serious IOI events

Study Limitations

Future research can address the following limitations: a lack of direct comparison of the durability of faricimab with durability of aflibercept, the short 1-year follow up period following primary endpoint analysis, and limitations of assessing the potential of faricimab to reduce treatment burden due to the required monthly visits from all patients to maintain masking.

Conclusions

This study with faricimab treatment intervals up to every 16-weeks achieved vision benefits and anatomical outcomes comparable with aflibercept every 8 weeks. This demonstrates that time between treatments can potentially be meaningfully extended with sustained efficacy in reducing treatment burden.