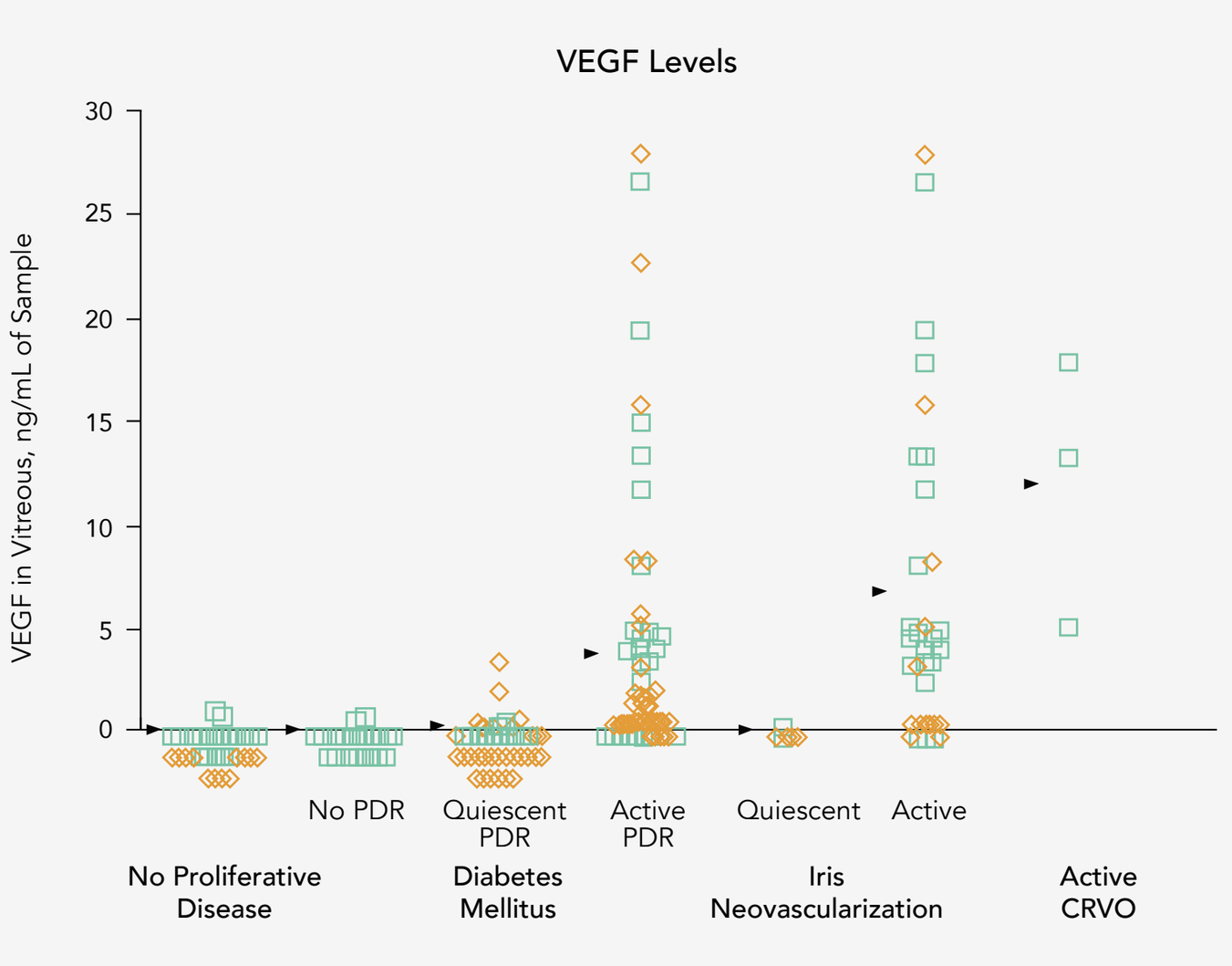
Faricimab in Neovascular Age-Related Macular Degeneration: Primary Results From the Phase 3 TENAYA and LUCERNE Trials

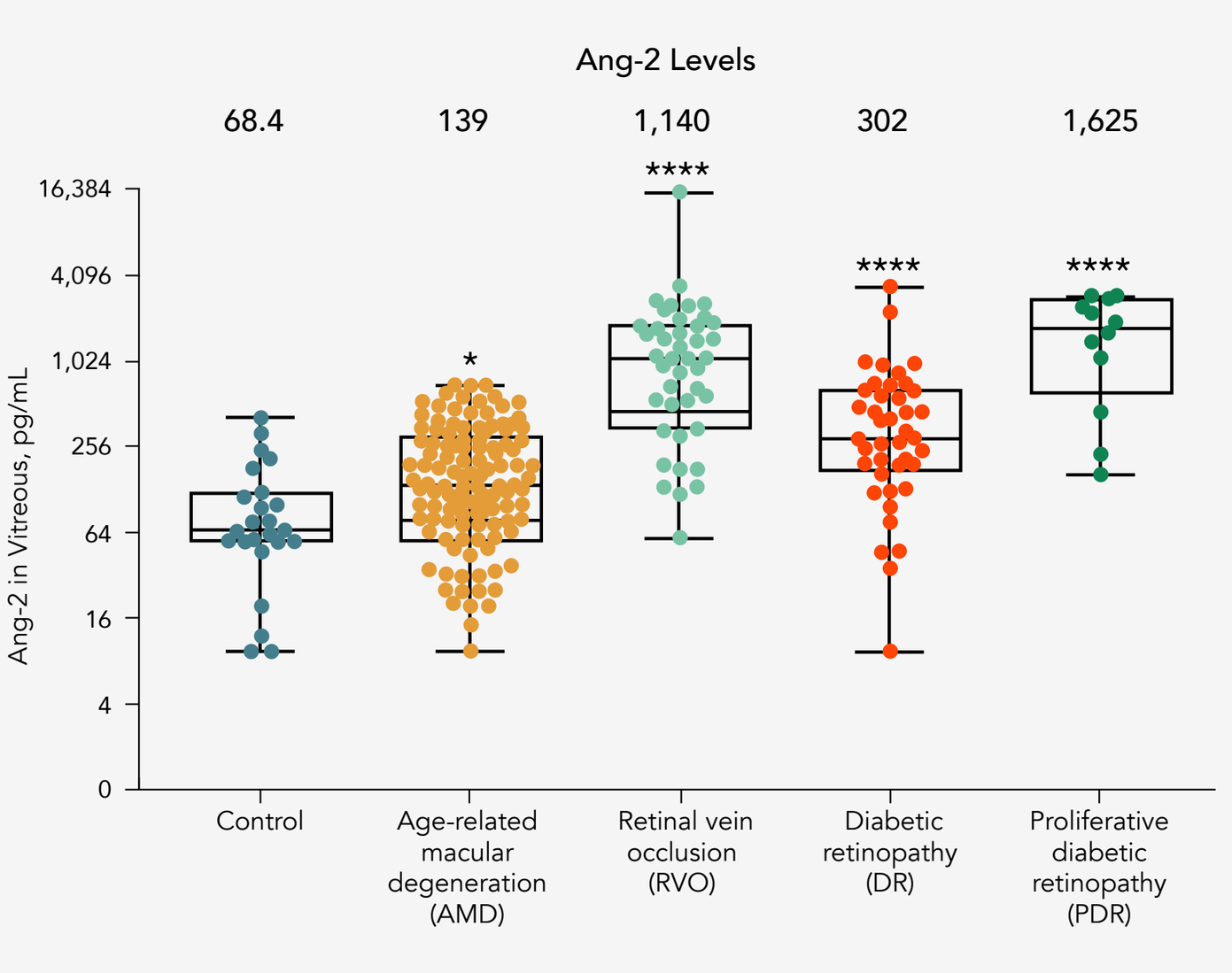
Singh RP, et al. Presented at the Annual Meeting of the American Academy of Ophthalmology (AAO); November 12-15, 2021.

Dual inhibition of angiopoietin-2 (Ang-2) and vascular endothelial growth factor (VEGF)-A with faricimab, a bispecific antibody designed for intraocular use, may promote vascular stability and durable efficacy in patients with neovascular age-related macular degeneration (nAMD). The primary results of the phase 3 TENAYA (NCT03823287) and LUCERNE (NCT03823300) trials are reported below.

Intraocular Ang-2 and VEGF levels are upregulated in retinal diseases.



Aiello LP, et al. *N Engl J Med.* 1994;331:1480-1487.



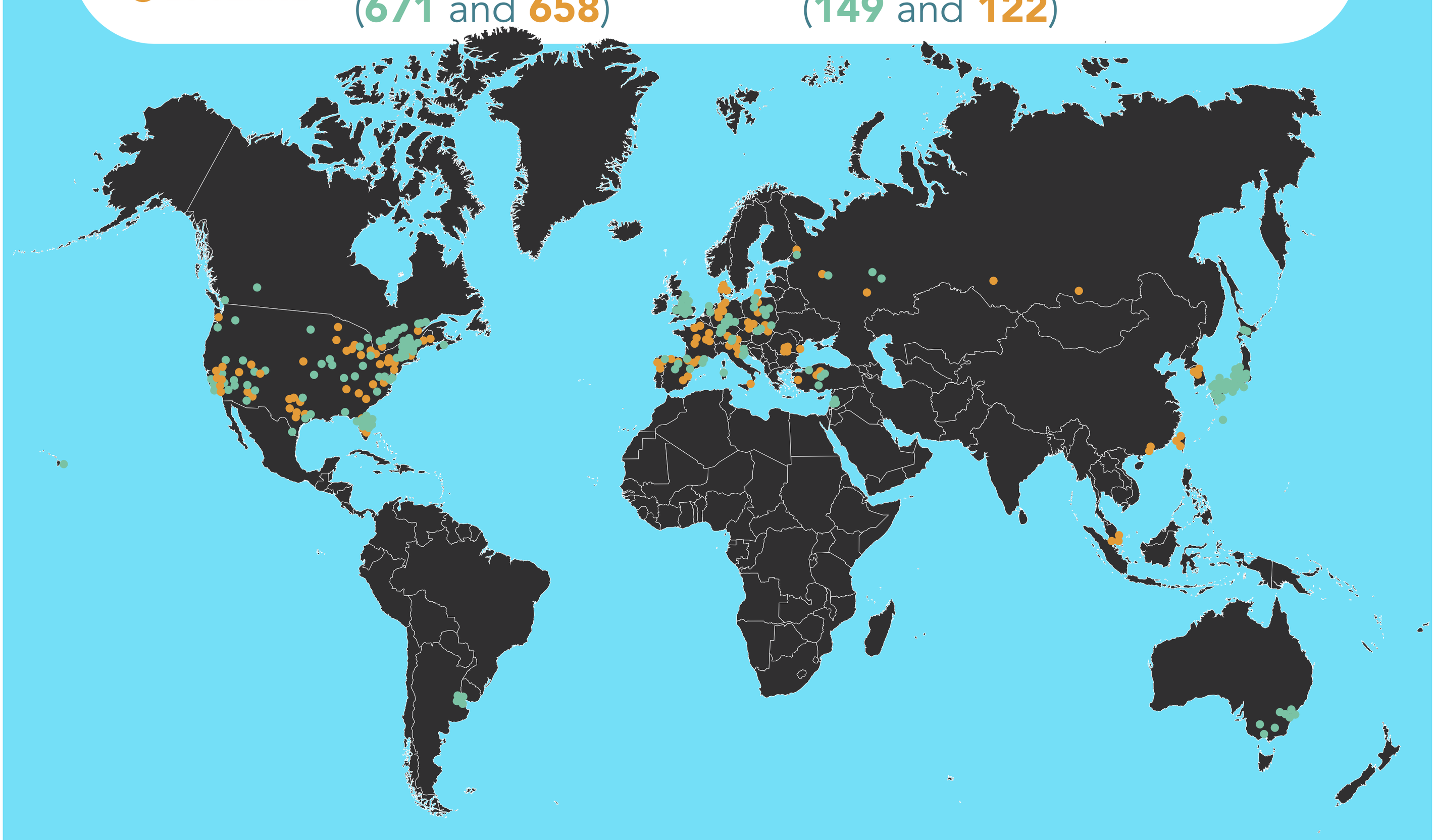
Human vitreous samples. * *P*< .05; **** *P*< .0001. A nonparametric Kruskal-Wallis analysis followed by Dunn's method for multiple comparisons was used to show significant differences of the groups to control, which are indicated by asterisks. Angiopoietin-1 (Ang-1) levels did not differ significantly, but Ang-2 levels were significantly different.

Regula JT, et al. *EMBO Mol Med.* 2016;8:1265-1288, with correction in Regula JT, et al. *EMBO Mol Med.* 2019;11:e10666.

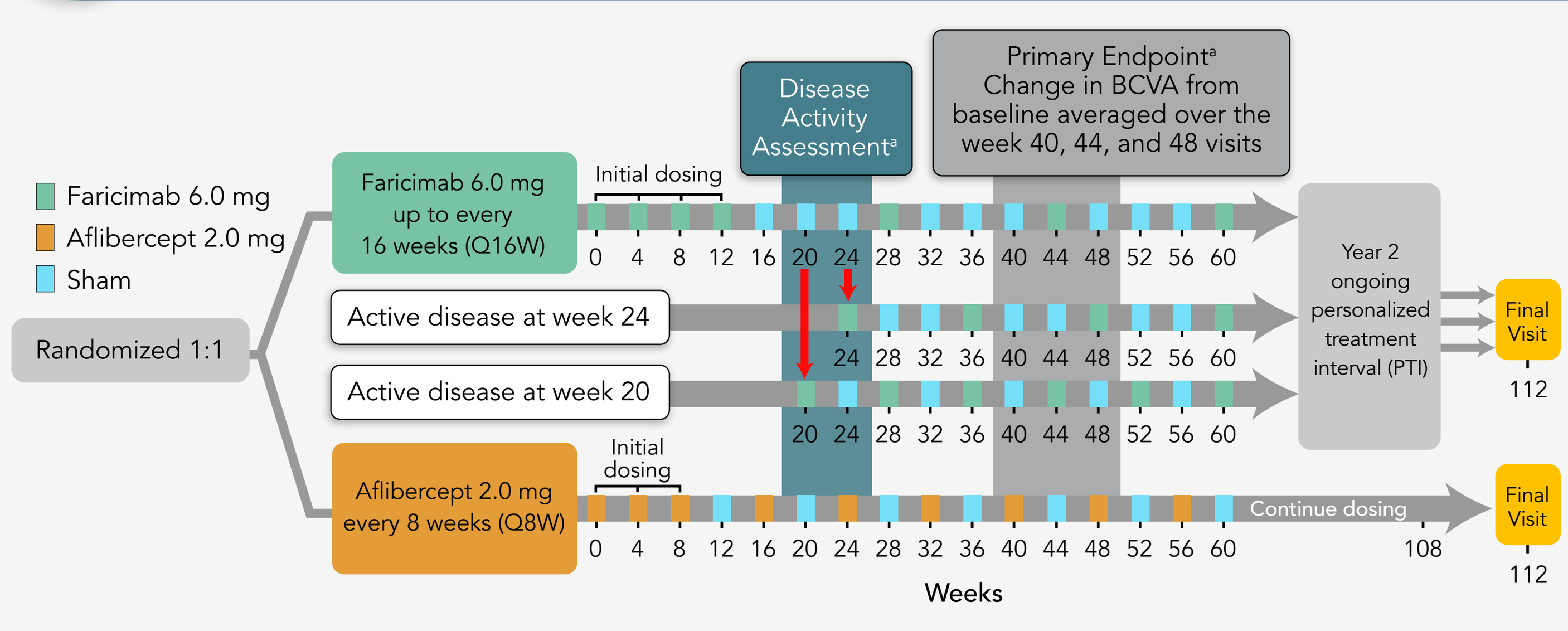
TENAYA and LUCERNE are 2 global phase 3 studies.

TENAYA
LUCERNE

1,329 patients enrolled (671 and 658) | **271** sites enrolled patients (149 and 122)



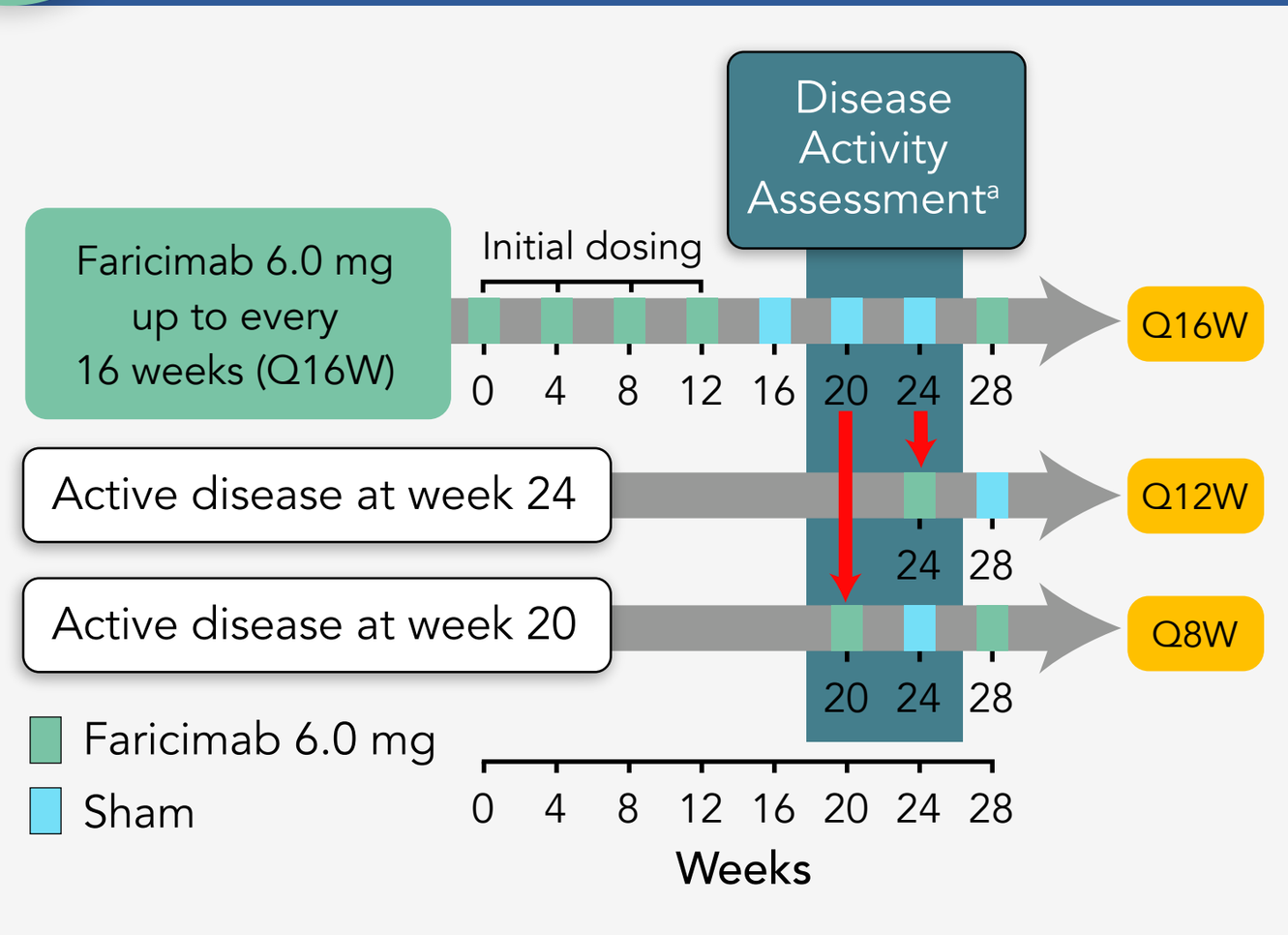
TENAYA and LUCERNE investigated faricimab using an individualized treatment interval of up to Q16W dosing.



- Treatment-naïve choroidal neovascularization (CNV) secondary to AMD (nAMD)
- Best-corrected visual acuity (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 Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart at a starting distance of 4 m.
[b] Identified by fundus fluorescein angiography (FFA) or optical coherence tomography (OCT).

Patients in the faricimab arm were assigned to Q16W, Q12W, or Q8W dosing intervals based on disease activity assessments.



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

Disease activity criteria (active disease if any are met)

Optical coherence tomography (OCT)
- Increase in central subfield thickness (CST) >50 μm compared with average CST over previous two scheduled visits[b]
- Increase in CST ≥75 μm compared with lowest CST recorded at either of previous two scheduled visits[b]

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

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

[a] Disease activity assessments at two time points helped ensure that patients in the faricimab arm received faricimab dosing according to their individual treatment needs.
[b] CST values obtained at site were entered into the interactive voice or web-based response system (IxRS) at weeks 12, 16, 20, and 24 for the determination of disease activity.

Key baseline characteristics were generally well balanced across treatment arms.

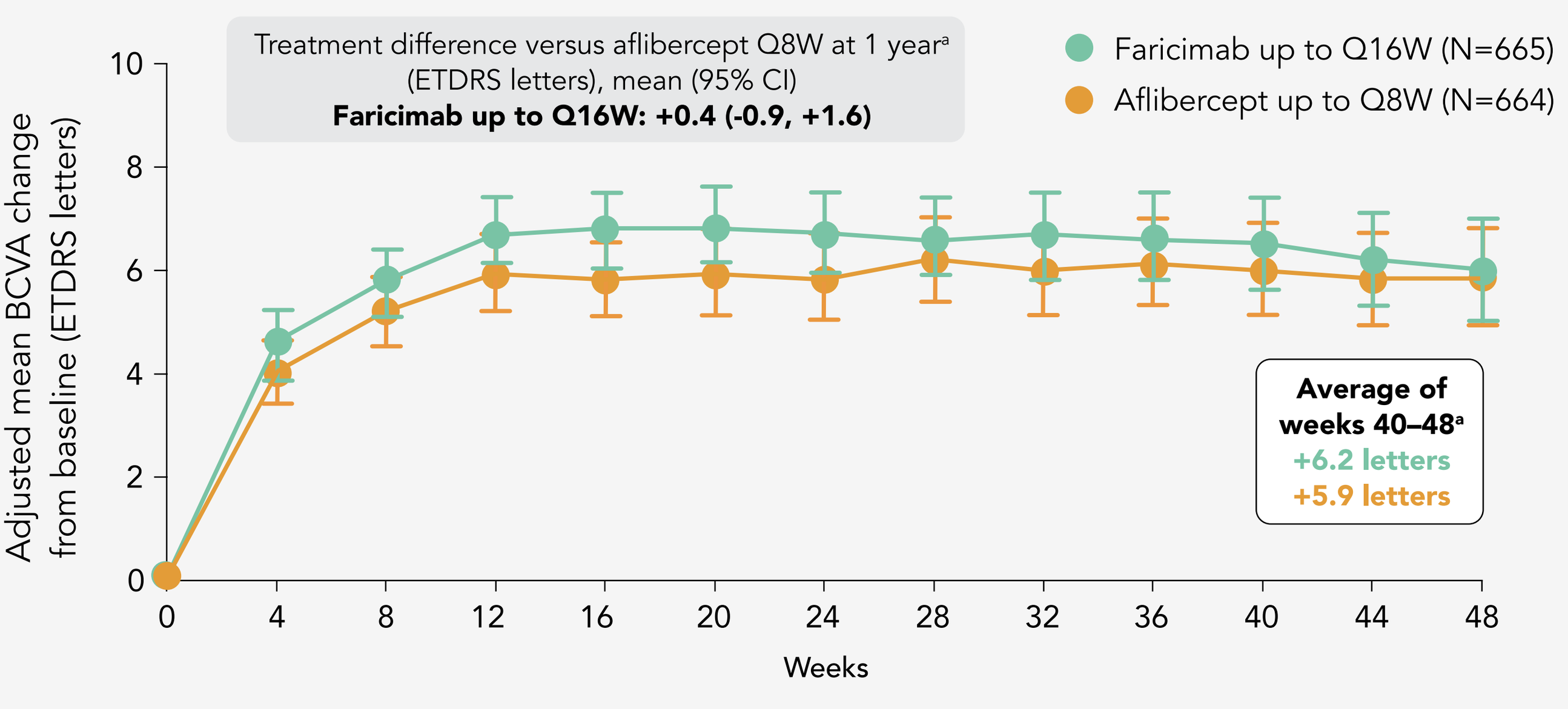
Intent-to-treat (ITT) population — **TENAYA/LUCERNE Pooled**

Intent-to-treat (ITT) population	Faricimab up to Q16W (N=665)	Aflibercept up to Q8W (N=664)
Age, years, mean (SD)	8.5%	8.7%
Sex: Female (%)	59.2%	60.1%
Race (%)[a]: White	87.4%	86.1%
BCVA, ETDRS letters, mean (SD)	13.3%	13.1%
CST, μm, mean (SD)[b]	122.1%	119.4%
Phakic (%)	57.6%	55.6%
Presence of intraretinal fluid (IRF) (%)	43.3%	46.8%
Presence of subretinal fluid (SRF) (%)	65.7%	67.3%
CNV location by FFA (%): Subfoveal	61.7%	56.8%
CNV location by FFA %): Juxtafoveal	24.2%	25.9%
CNV location by FFA (%): Extrafoveal	12.5%	14.9%

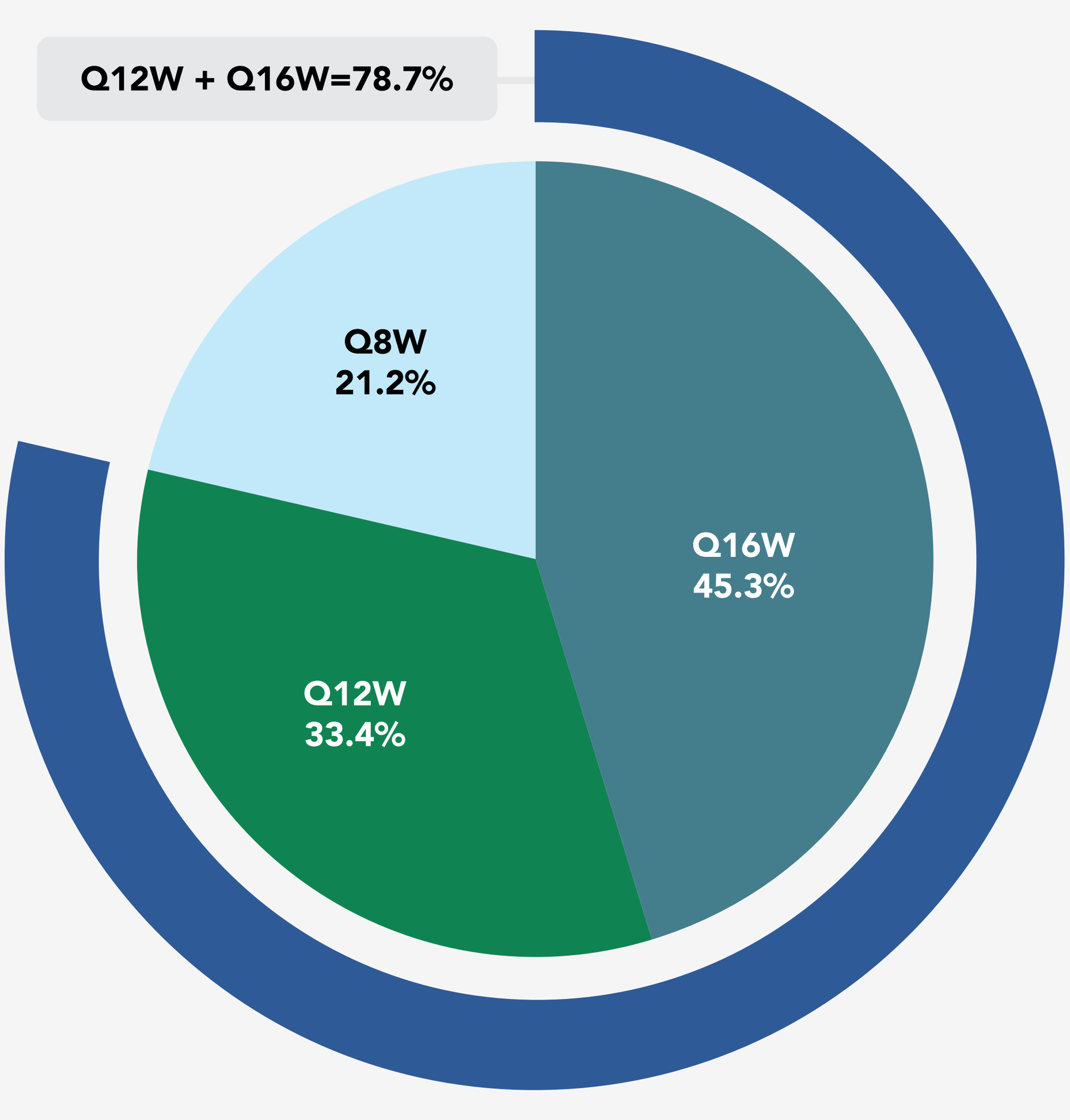
[a] Not all race categories are presented; percentages do not add up to 100. Age is at randomization.
[b] CST is measured as internal limiting membrane (ILM)-retinal pigment epithelium (RPE).

Faricimab demonstrated durable vision gains at week 48 with ~45% of patients on Q16W and almost 80% on ≥Q12W dosing.

TENAYA/LUCERNE Pooled



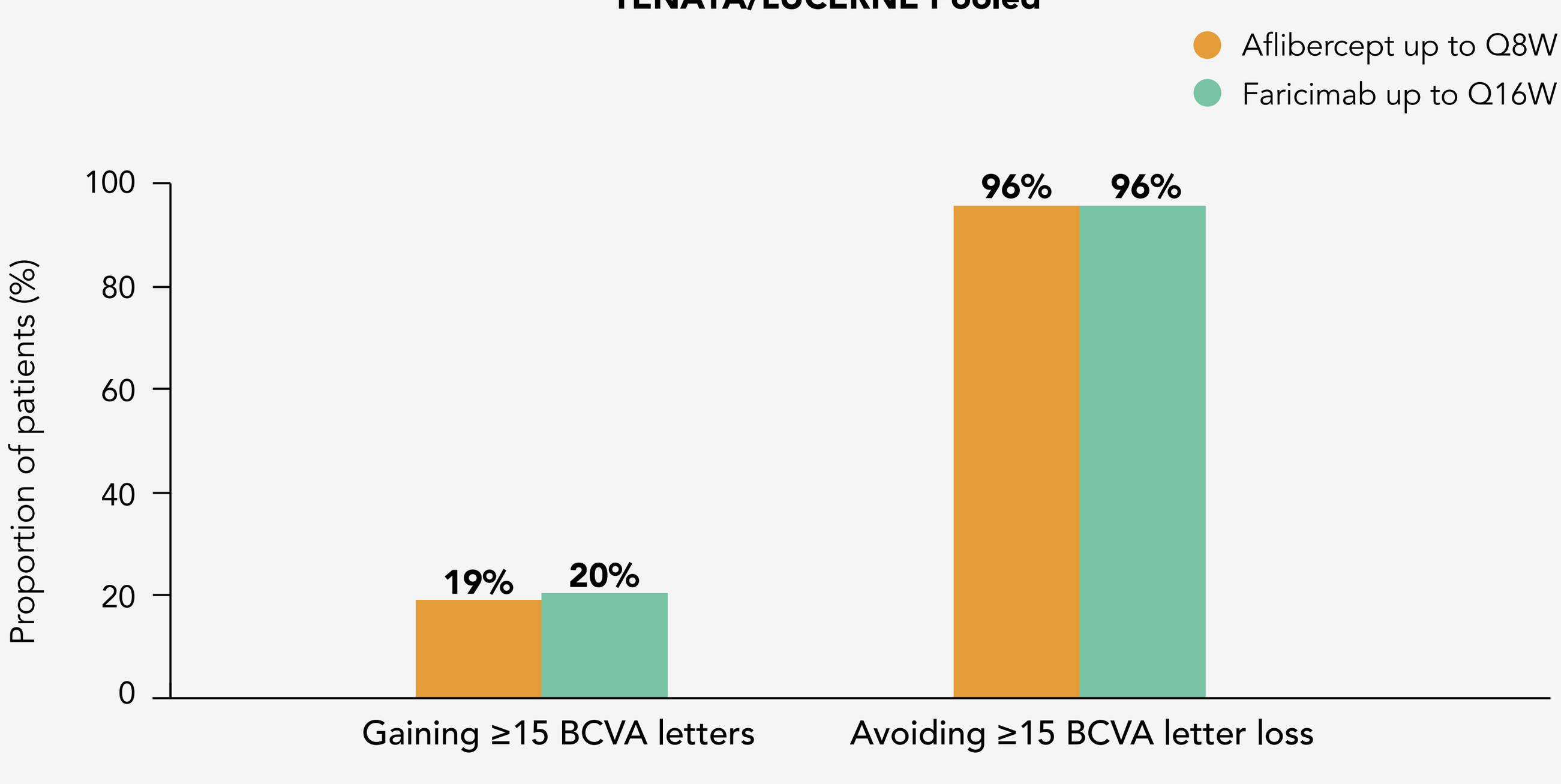
TENAYA/LUCERNE Pooled (N=665)[b]



[a] Adjusted mean BCVA change from baseline at 1 year, averaged over weeks 40, 44, and 48. Results are based on a mixed model for repeated measures analysis in the ITT population. 95% CIs are shown.
[b] 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.

Faricimab up to Q16W resulted in a comparable proportion of patients gaining or maintaining vision[a] as with aflibercept Q8W.

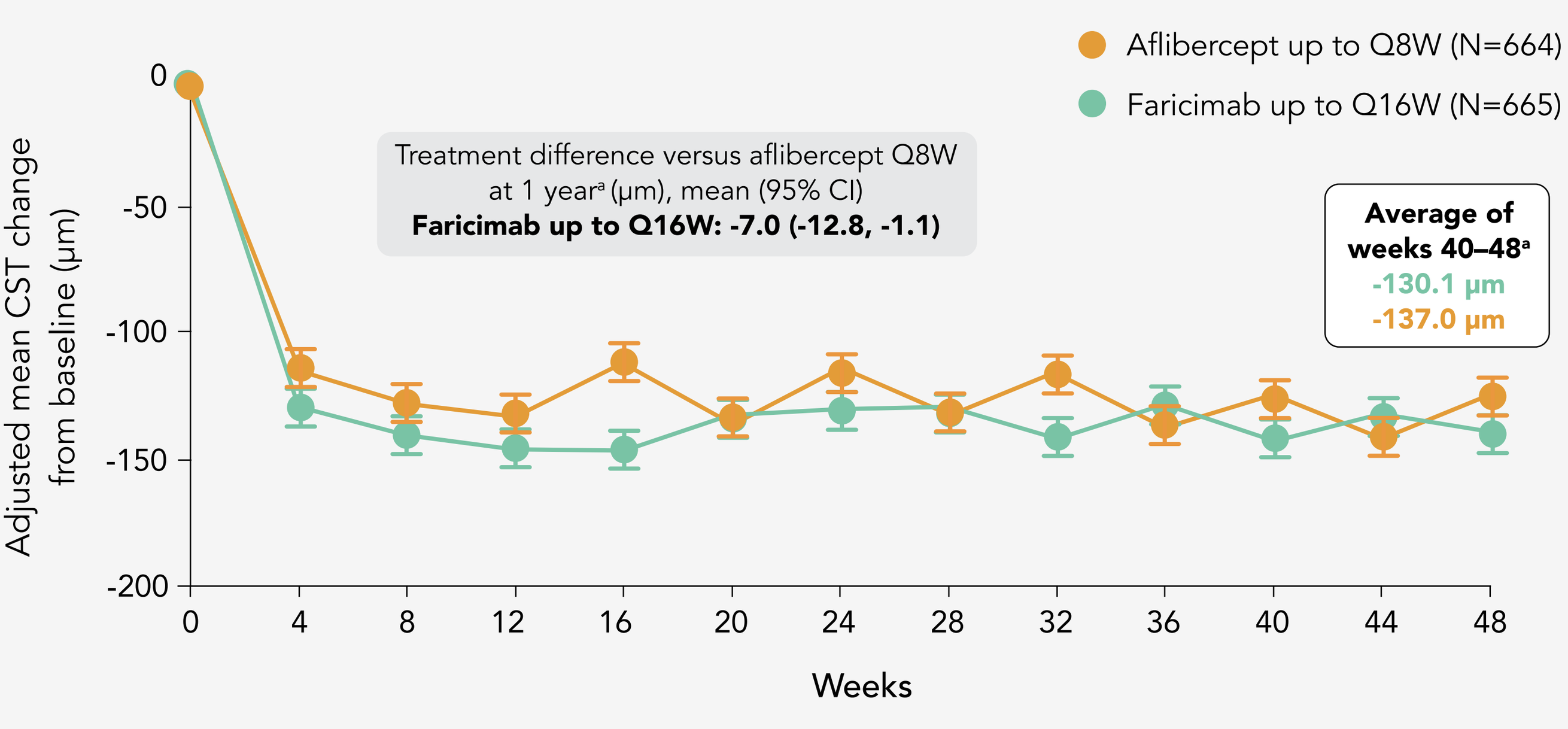
TENAYA/LUCERNE Pooled



Includes patients with ≥1 nonmissing assessment at weeks 40, 44, and 48 (TENAYA/LUCERNE pooled: aflibercept Q8W, n=591; faricimab up to Q16W, n=594). Proportion of patients in each group was estimated using the Cochran-Mantel-Haenszel method (95% 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.

Faricimab up to Q16W resulted in meaningful and comparable central subfield thickness (CST) reductions vs aflibercept Q8W.

TENAYA/LUCERNE Pooled



Results are based on a mixed model for repeated measures analysis. 95% CIs are shown. CST is measured as ILM-RPE, as graded by central reading center.
[a] Adjusted mean CST change from baseline at 1 year, averaged over weeks 40, 44, and 48.

Low rates of ocular adverse events (AEs) were found in the study eye through week 48 and no cases of retinal vasculitis were reported.

Common ocular AEs through week 48 — **TENAYA/LUCERNE Pooled**

Common ocular AEs through week 48	Faricimab up to Q16W (N=664)	Aflibercept up to Q8W (N=662)
Patients with any events (%)	38.3%	37.2%
Conjunctival hemorrhage (%) (*Most common event*)	6.8%	7.7%

Results are presented based on the safety-evaluable population. Common ocular AEs defined as those occuring in >2% of any arm. All events are investigator reported. Percentages are based on n in the column headings.
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).

Low rates of adverse events of intraocular inflammation (IOI) were found.

101 events through week 48 — **TENAYA/LUCERNE Pooled**

101 events through week 48	Faricimab up to Q16W (N=664)	Aflibercept up to Q8W (N=662)
Patients with amy AEs of IOI (excluding endophthalmitis) (%)	2.0%	1.2%
Iritis (%)	0.5%	0.3%
Uvetis (%)	0.3%	0.3%
Keratic precipitates (%)	0.2%	0%
Vitritis (%)	0.5%	0.2%
Iridocyclitis (%)	0.5%	0.3%
Choriotentinitis (%)	0.2%	0%
Post-procedural inflammation	0%	0.2%
Endophthalmitis	0%	0.2%

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).

Conclusions

Pooled data from TENAYA and LUCERNE demonstrated durable efficacy with faricimab up to Q16W dosing. Dual inhibition of Ang-2 and VEGF-A with faricimab may promote vascular stability, providing more durable therapy while maintaining long-term vision gains. BCVA improvement was found with ~45% of patients on Q16W and almost 80% on ≥Q12W dosing at week 48. Meaningful reductions in CST with faricimab up to Q16W were 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.