Key Clinical and Anatomical Outcomes With Faricimab in Patients With nAMD: Results From the TENAYA/LUCERNE Trials

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Disclosures

Financial Disclosures

- RLA: Consultant: 4DMT, AbbVie, Adverum, Alcon, Alimera, Allergan, Amgen, Apellis, AsclepiX, Astellas, Bausch + Lomb, Cardinal Health, Clearside Biomedical, Coherus, EyePoint, ForwardVue, Genentech, Inc., Glaukos, Imprimis, InFocus Capital Partners, Ingenia, Kriya, KYS Vision, Merit, Notal Vision, Novartis, NVasc, Ocular Therapeutix, OcuTerra, Opthea, Outlook, Pixium, Pr3vent, PulseMedica, Regenxbio, Replenish, Re-Vana, Sandoz, Santen, Tenpoint Therapeutics, Vial, Visionary Ventures; Stock: AbbVie, Adverum, Alcon, Aldeyra, Apellis, EyePoint, InFocus Capital Partners, Iveric Bio, Kodiak Sciences, Novartis, NVasc, Ocular Therapeutix, Outlook, Regeneron, Replenish, Re-Vana, Verana Health, Visionary Ventures; Stock Options: Aviceda, ForwardVue, Ingenia, KYS Vision, NVasc
- MA, IS, MY: Employee: Genentech, Inc.
- AK: Employee: Roche Products Ltd.
- PM: Employee: F. Hoffmann-La Roche Ltd.

Study and Product Disclosures

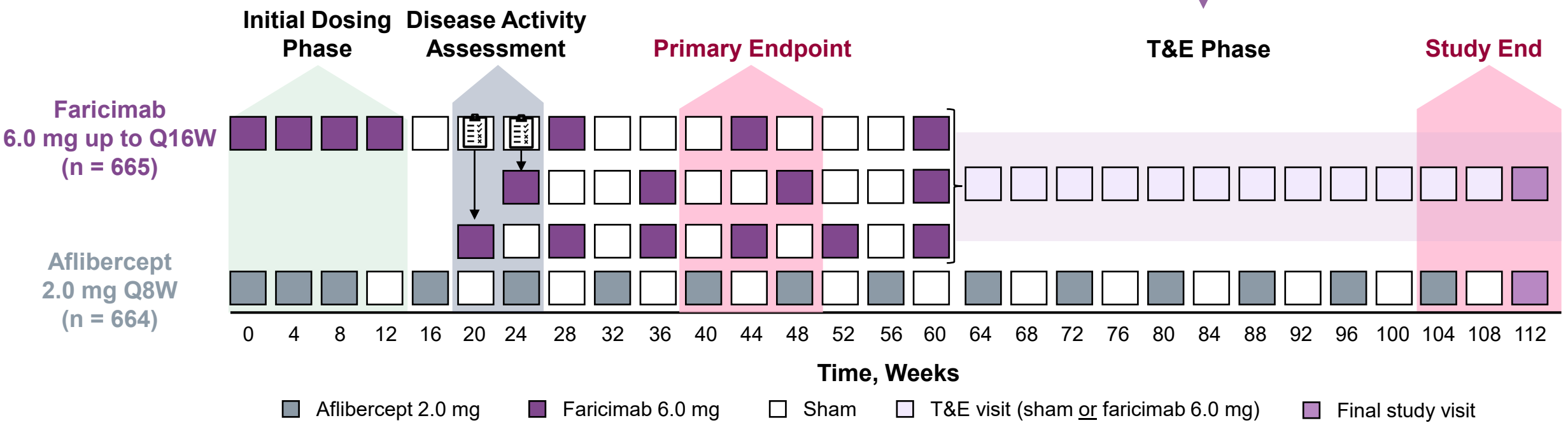
- Faricimab is approved for the treatment of neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion in multiple countries worldwide and is not currently approved for use outside these indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and third-party writing assistance, which was provided by Gary Vang, PharmD, of Envision Pharma Group

TENAYA and LUCERNE Trial Design

Faricimab nAMD Trials Use Disease Criteria Reflective of Clinical Practice

Disease activity assessment criteria
(at weeks 20 and 24) based on
CST OR BCVA OR new macular hemorrhage

T&E Regimen (PTI per Protocol)
Dosing, based on defined criteria:
Extended **Reduced** **Maintained**

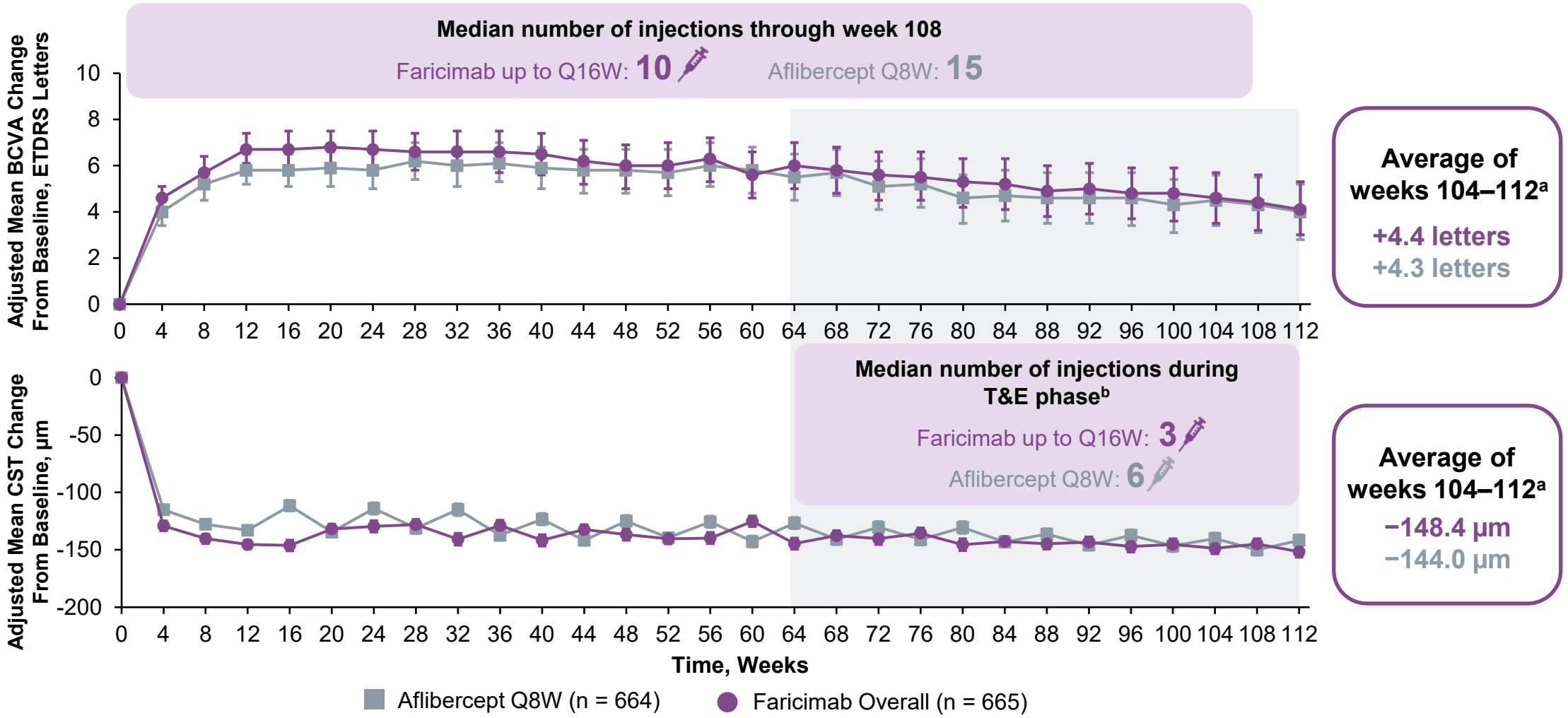


T&E regimen in TENAYA (NCT03823287) and LUCERNE (NCT03823300) uses different criteria than those used in the YOSEMITE and RHINE clinical trials. [a] Per the investigator. BCVA, best-corrected visual acuity; CST, central subfield thickness; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

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

ITT population

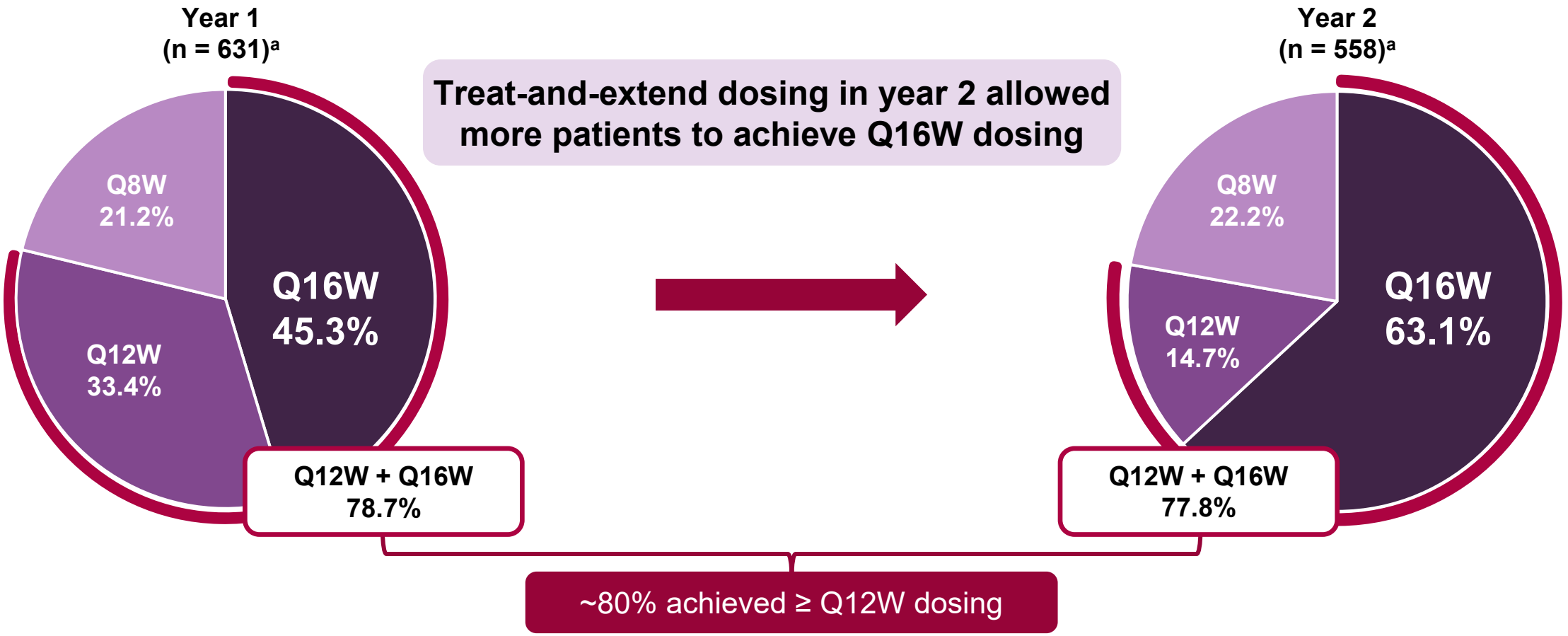
TENAYA/LUCERNE Pooled



Results are based on a MMRM analysis in the ITT population. For the MMRM analysis, the model is adjusted for treatment group, visit, visit-by-treatment group interaction, baseline BCVA (continuous), baseline BCVA (≥ 74 letters, 73–55 letters, and ≤ 54 letters), baseline LLD (< 33 letters and ≥ 33 letters), and region (US and Canada, Asia, and the rest of the world), and study (TENAYA vs LUCERNE). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19–related and COVID-19–related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 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 center. [a] Adjusted mean change from baseline at 2 years, averaged over weeks 104, 108, and 112. [b] T&E phase refers to the protocol-driven personalized treatment interval. After week 60 to week 112, faricimab treat-and-extend phase vs aflibercept Q8W fixed dosing. Based on study design, aflibercept 2.0 mg was not allowed to extend beyond Q8W dosing. T&E dosing regimen was delayed in some patients due to dose holds or missed visits. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; ITT, intent to treat; LLD, low luminance deficit; MMRM, mixed model for repeated measures; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; T&E, treat-and-extend.

~80% of Faricimab-Treated Patients Achieved ≥ Q12W Dosing at the End of the Second Year

TENAYA/LUCERNE Pooled



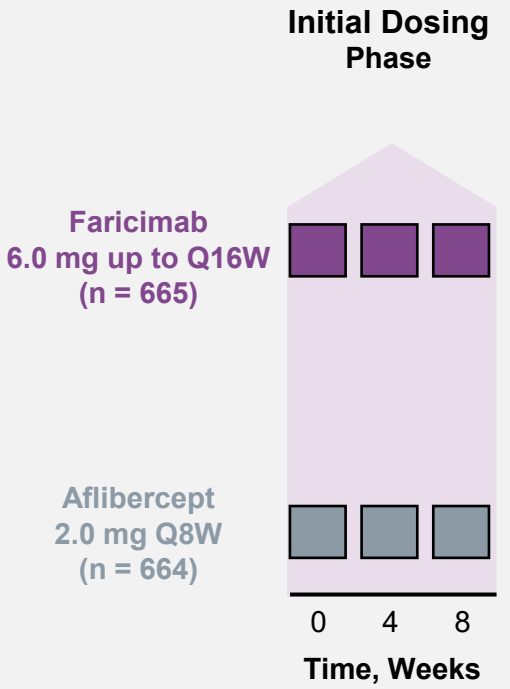
[a] Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at that visit. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Interval at year 2 is calculated using data recorded at week 108. Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

Greater Anatomic Improvements During H2H Phase With Faricimab vs Aflibercept

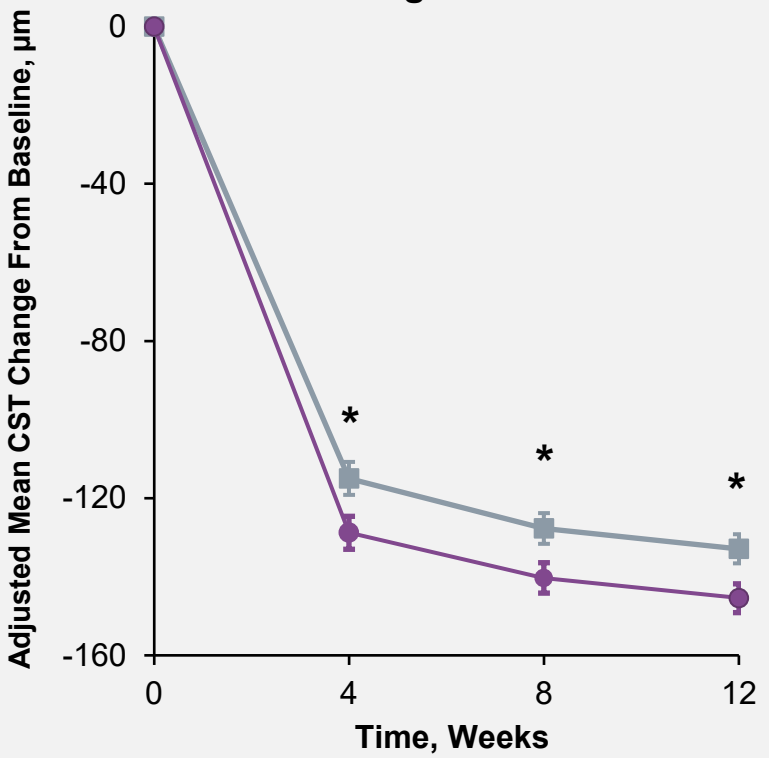
ITT population

TENAYA/LUCERNE Pooled: Post Hoc Analysis

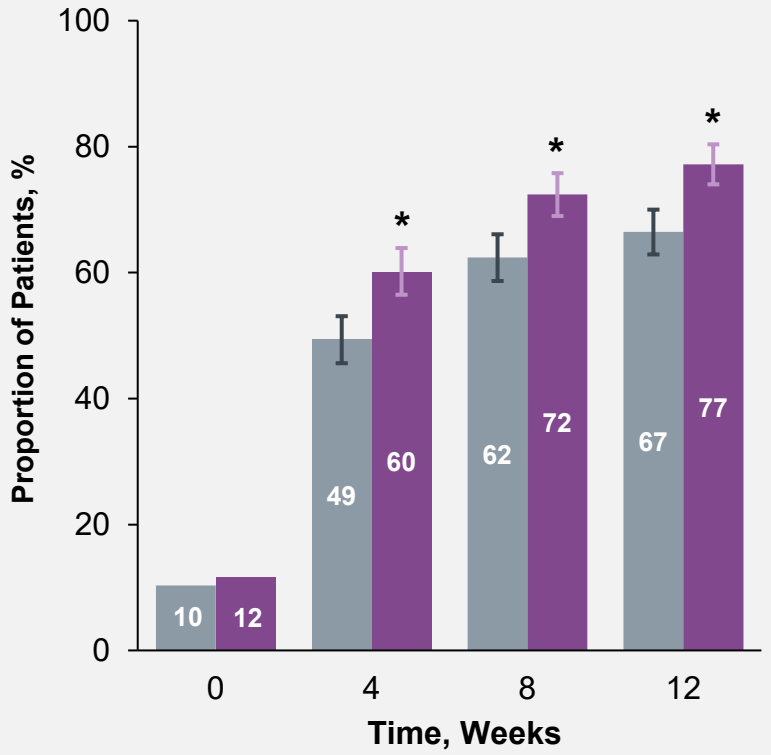
Head-to-Head Dosing Phase



CST Change From Baseline



Absence of SRF and IRF[a]



Aflibercept (n = 664) Faricimab (n = 665)

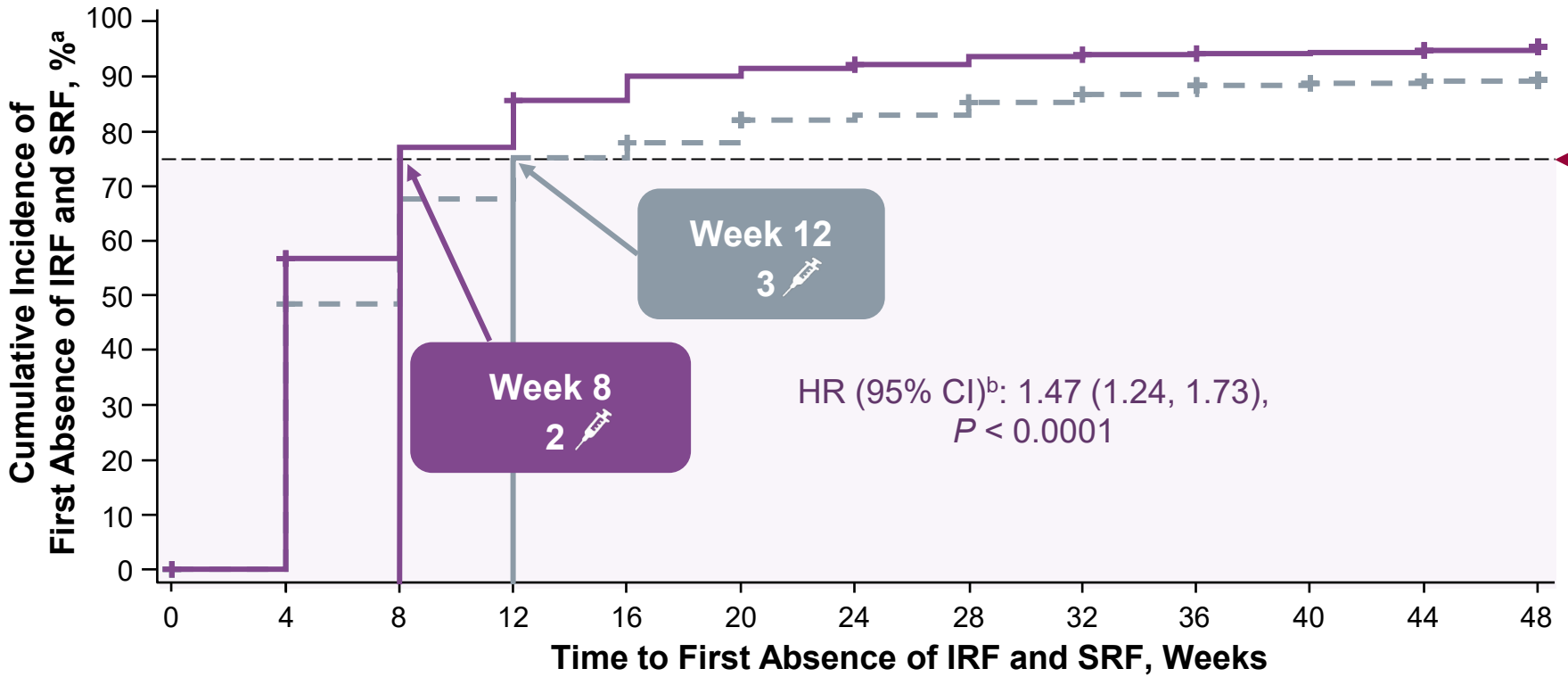
* Nominal $P \leq 0.0001$ vs aflibercept

TENAYA (NCT03823287); LUCERNE (NCT03823300). 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 center. *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. [a] IRF and SRF are as measured in the central subfield (center 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 (TENAYA vs LUCERNE). 95% CIs are shown and estimates < 0% or > 100% are imputed as 0% or 100%, respectively. BCVA, best-corrected visual acuity; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; 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.

Faster First Absence of IRF and SRF With Fewer Injections With Faricimab

Patients with IRF and/or SRF at baseline

TENAYA/LUCERNE Pooled: Post Hoc Analysis



75th percentile: 4 weeks earlier with faricimab vs aflibercept

47% increase chance of drying the retina with faricimab vs aflibercept

Median number of injections[c]

Aflibercept Q8W	591	587	302	190	146	129	101	96	82	73	61	57	54
Faricimab up to Q16W	581	577	248	132	82	57	49	44	36	33	31	30	25

Summaries of time to first absence of IRF and SRF are Kaplan-Meier estimates, with the time variable defined as the target visit week. Patients with absence of IRF and SRF at baseline and patients with no data at baseline were excluded from the analysis. *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. [a] Event is defined as the first absence of IRF and SRF after randomization 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 (TENAYA vs LUCERNE). HRs were estimated by Cox regression. An HR > 1 favors faricimab over aflibercept. [c] The number of injections includes any active drug administered (faricimab or aflibercept), including medication errors. BCVA, best-corrected visual acuity; CI, confidence interval; HR, hazard ratio; IRF, intraretinal fluid; LLD, low-luminance deficit; Q8W; every 8 weeks; Q16W, every 16 weeks; SRF, subretinal fluid.

Greater Reduction in Max PED Thickness and Fewer Remaining Serous PED With Faricimab vs Aflibercept at Week 12

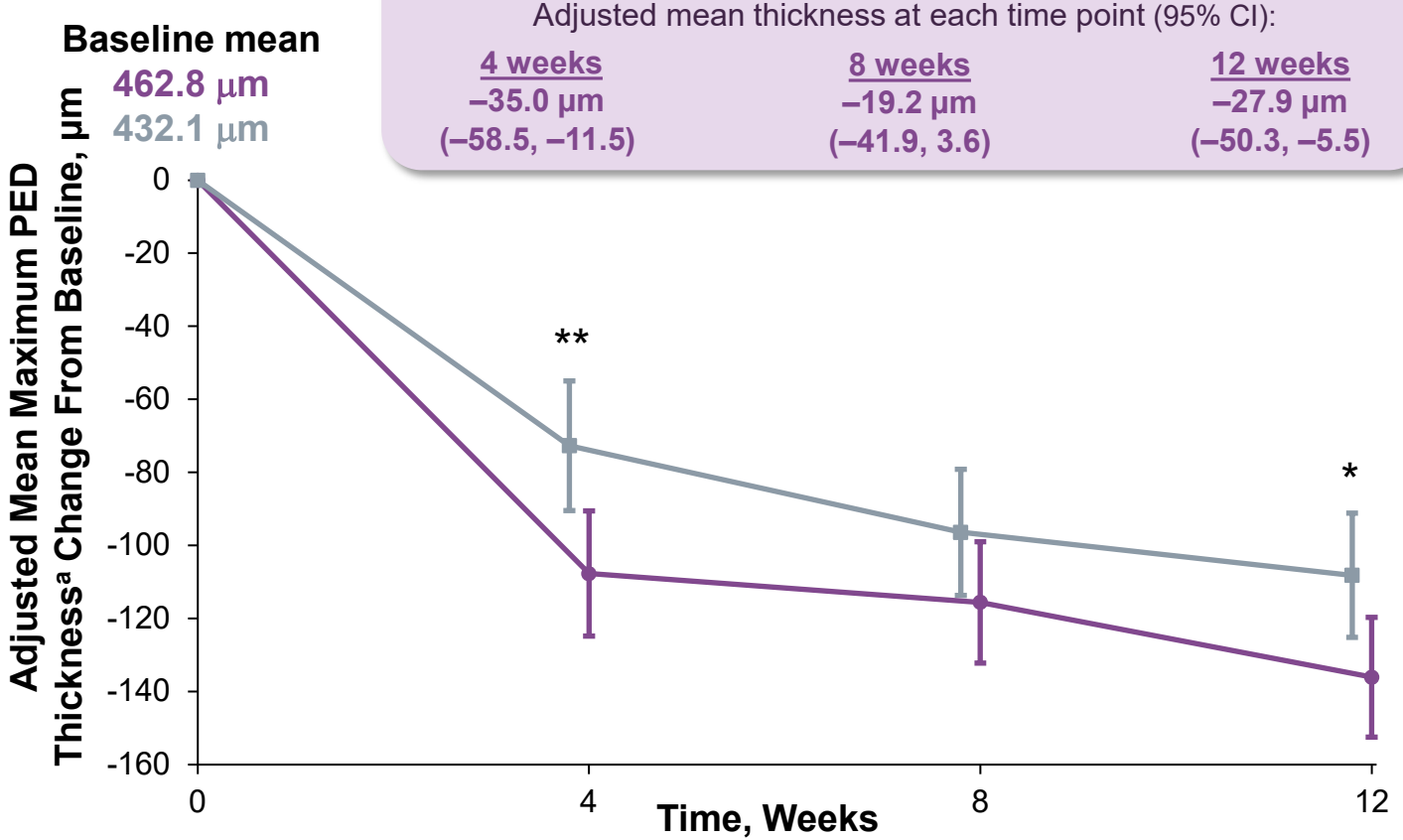
In Patients With Presence of Serous PED at Baseline

TENAYA/LUCERNE Pooled: Post Hoc Analysis

Difference vs aflibercept

Adjusted mean thickness at each time point (95% CI):

4 weeks	8 weeks	12 weeks
–35.0 µm	–19.2 µm	–27.9 µm
(–58.5, –11.5)	(–41.9, 3.6)	(–50.3, –5.5)



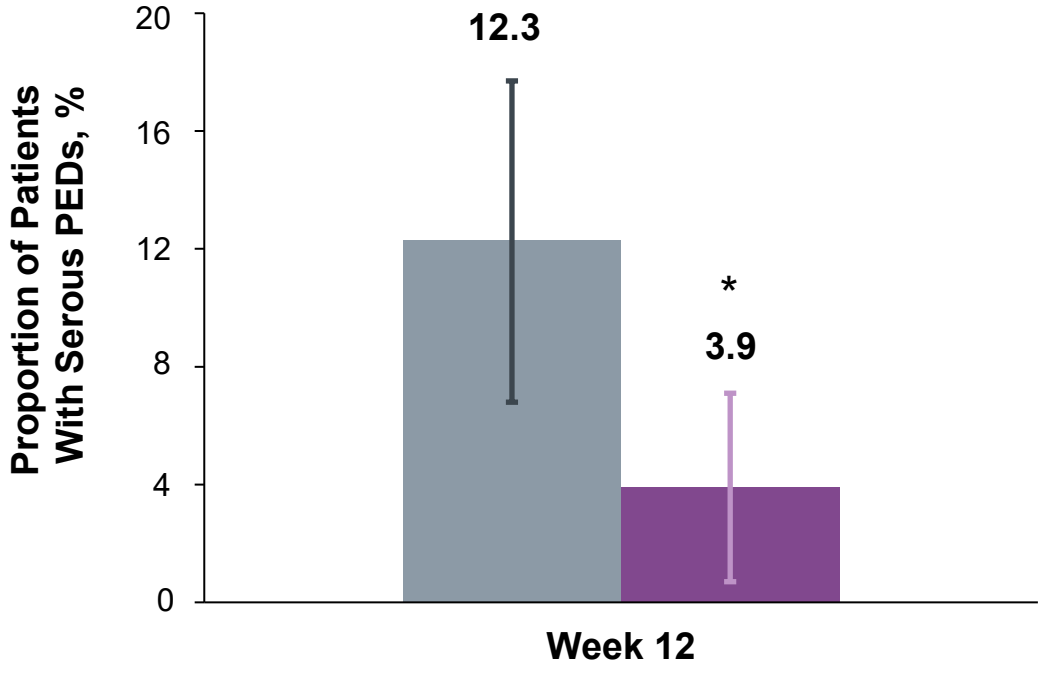
* Nominal $P < 0.05$ vs aflibercept
** Nominal $P < 0.01$ vs aflibercept

Aflibercept (n = 114) Faricimab (n = 128)

Difference vs aflibercept

–8.4%

(95% CI, –14.7, –2.0)



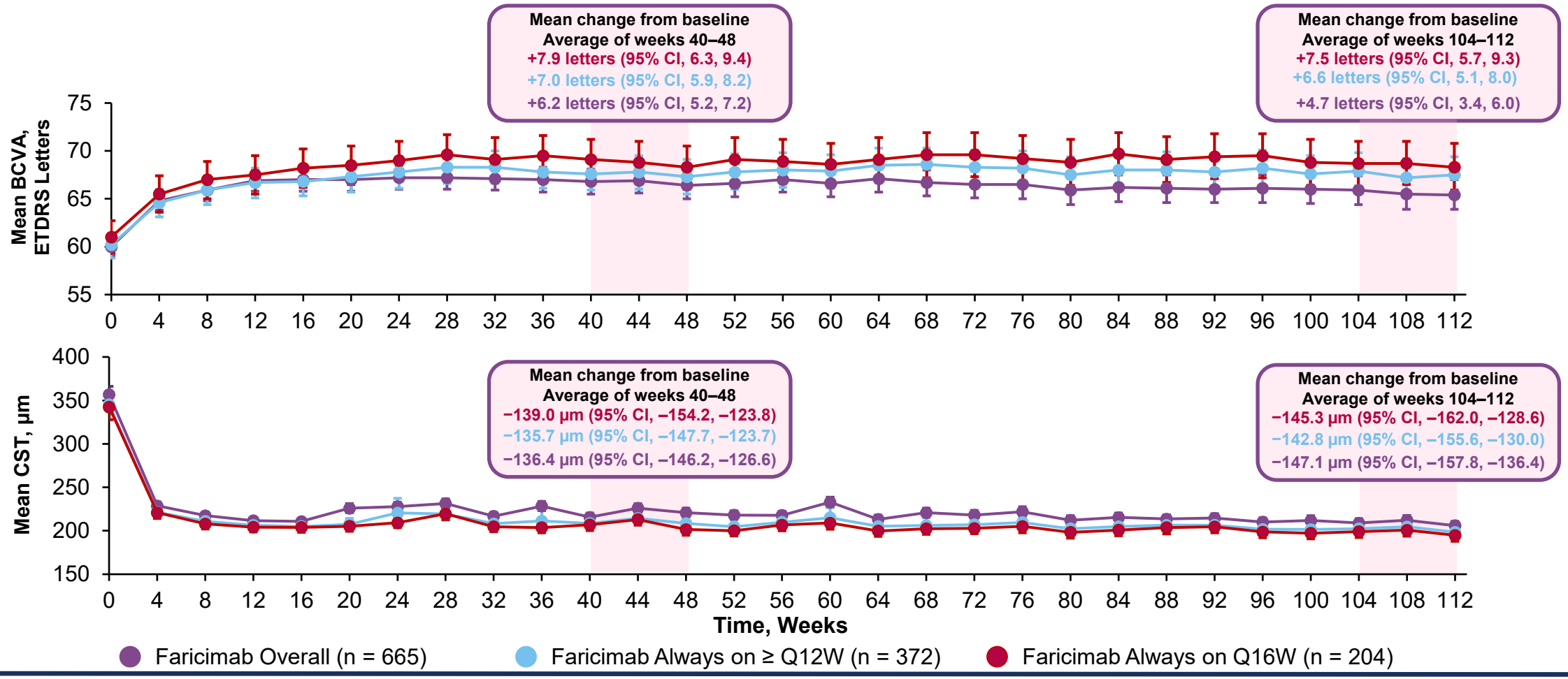
Aflibercept (n = 112) Faricimab (n = 127)

Predominantly serous and serous PEDs are reported as serous PED. CMH-weighted estimates are reported. * Nominal $P < 0.05$ vs aflibercept; ** Nominal $P < 0.01$ vs aflibercept. *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. [a] Within the 6-mm ETDRS grid. PED thickness results are based on a mixed model for repeated measures analysis in the ITT population adjusted for treatment group, visit, visit-by-treatment group interaction, baseline PED (continuous), PED type at baseline (fibrovascular vs serous), baseline BCVA (≥ 74, 73–55, and ≤ 54 letters), baseline LLD (< 33, ≥ 33 letters), region (United States and Canada, Asia, and the rest of the world), reading center (Vienna vs Duke), and study (TENAYA vs LUCERNE). Treatment policy strategy and hypothetical strategy were applied to non–COVID-19–related and COVID-19–related intercurrent events, respectively. 95% CIs are shown. Presence of PED defined as measured maximum thickness of PED within 6-mm ETDRS grid at baseline. BCVA, best-corrected visual acuity; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; ETDRS, Early Treatment Diabetic Retinopathy Study; H2H, head-to-head; ITT, intent to treat; LLD, low-luminance deficit; PED, pigment epithelial detachment.

Patients Always on Extended Dosing Achieved Stable BCVA Gains and CST Reductions Through 2 Years

TENAYA/LUCERNE Pooled: Post Hoc Analysis

Median number of injections from week 24[a]: **6**

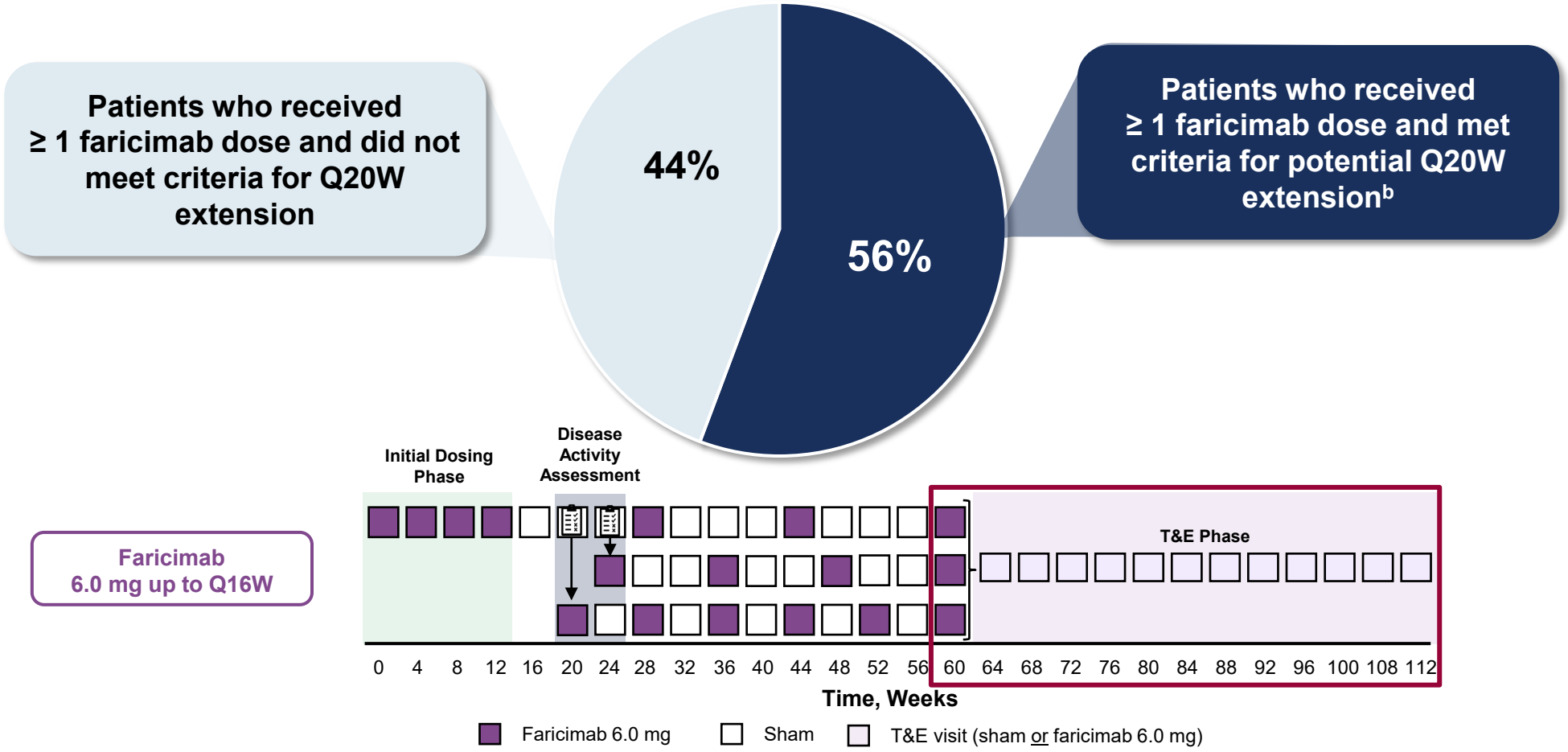


Patients were analyzed as randomized (ITT principle) and were included in the analysis through completion/discontinuation. Baseline is defined as the last available value on or prior to randomization. 95% CIs are shown. The median number of injections is based on the safety-evaluable population. CST was measured as ILM-RPE, as graded by central reading center. [a] Median number of injections for patients treated with faricimab up to Q16W and faricimab always on ≥ Q12W. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; ITT, intent to treat; Q12W, every 12 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium.

> 50% of Faricimab-Treated Patients Met Criteria for Potential Q20W Dosing in the T&E phase

TENAYA/LUCERNE Pooled: Post Hoc Analysis

n = 591[a]



[a] Limited to patients who received ≥ 1 faricimab dose during the T&E phase. [b] The same protocol defined extension criteria for personalized T&E was used in this analysis.
Q16W, every 16 weeks; Q20W, every 20 weeks; T&E, treat-and-extend.

Faricimab Was Well Tolerated With a Safety Profile Comparable to Aflibercept

AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	TENAYA/LUCERNE Pooled	
	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
Noninfectious 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)[f]	0
Serious nonocular AEs	138 (20.8)	162 (24.5)
APTC events[e]	22 (3.3)	20 (3.0)

[a] Results are presented for the pooled 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] APTC events were adjudicated by an external independent committee; all other events were investigator reported. [f] Hollenhorst plaque that was reported at the end of year 1 and was not treatment-related as per the investigator. AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; Q8W, every 8 weeks; Q16W, every 16 weeks.

Clinical Pearls From the TENAYA/LUCERNE Trials Demonstrated Robust Disease Control and Extended Durability Through Dual Ang-2/VEGF-A Inhibition With Faricimab

- Robust and stable vision gains and anatomic improvements through 2 years

- Biomarkers (CST, retinal fluid, PED) demonstrated greater anatomic improvements with faricimab vs aflibercept during the H2H dosing phase

- Patients on extended dosing achieved stable outcomes, highlighting potential for further interval extension

Ang-2, angiopoietin-2; CST, central subfield thickness; H2H, head-to-head; PED, pigment epithelial detachment; VEGF-A, vascular endothelial growth factor-A.