# Greater Reduction in Pigment Epithelial Detachment Size With Faricimab vs Aflibercept During Head-to-Head Dosing in Patients With nAMD

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## Purpose

This post hoc analysis of pooled patient data from the phase 3 TENAYA and LUCERNE trials assessed the impact of faricimab vs aflibercept on pigment epithelial detachment (PED) during head-to-head (H2H) dosing

## Conclusions

In the H2H phase of TENAYA and LUCERNE, dual angiopoietin-2 (Ang-2)/vascular endothelial growth factor (VEGF)-A inhibition with faricimab elicited greater improvement in PED outcomes vs VEGF inhibition alone with aflibercept

These findings are consistent with the greater and faster drying of retinal fluid seen over the same time period in these trials as evidenced by retinal biomarkers (central subfield thickness [CST], intraretinal fluid [IRF] and subretinal fluid [SRF]) and which may allow for rapid interval extension

There was a higher number of retinal pigment epithelial tears with faricimab compared with aflibercept (not clinically or statistically significant)

### Financial Disclosures

- AL: Travel Support: Roche; Equity: EyeBio
- PM, AS: Employee: F. Hoffmann-La Roche Ltd.
- MY, YS, JRW, SP: Employee: Genentech, Inc.
- AK: Employee: Roche Products Ltd.

### Study and Product Disclosures

- In the UK, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema. Faricimab is not currently approved for use outside these indications in the UK
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
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- Roche conducted a factual accuracy check on the final article but any decision to incorporate comments was made solely at the discretion of the authors

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## Background

- In the H2H phase of the TENAYA/LUCERNE (NCT03823287/NCT03823300) neovascular age-related macular degeneration (nAMD) trials, dual inhibition of Ang-2 and VEGF-A with faricimab led to greater reduction in CST and an increase in absence of SRF and IRF vs aflibercept[1,2]
- PED is a relatively common complication in patients with nAMD[3]
- PED occurs when the retinal pigment epithelium (RPE) detaches from the Bruch's membrane due to a build-up of fluid, fibrovascular membrane, blood or drusenoid material[3]
- Sub-RPE fluid is more persistent than IRF and SRF in nAMD and PED in nAMD requires consistent anti-VEGF therapy and can recur during as-needed treatment[4,5]

## Methods

- Treatment-naïve patients from TENAYA/LUCERNE (pooled N = 1329) were randomised 1:1 to faricimab 6.0 mg up to every 16 weeks (Q16W; n = 665) after 4 initial every-4-week (Q4W) doses or aflibercept 2.0 mg every 8 weeks (Q8W; n = 664) after 3 initial Q4W doses
- PED was defined as an RPE elevation with a width of ≥ 350 µm (to exclude drusenoid PEDs)
- PED was graded as predominantly serous or purely serous (serous PED) or predominantly fibrovascular or fibrovascular only (fibrovascular PED)
- Baseline PED characteristics and changes in maximum PED thickness during H2H dosing through week 12 were assessed, as well as time to first reduction of maximum PED thickness by 50% from baseline through year 1 in patients with PED ≥ 125 µm at baseline

### References

1. Heier JS et al. *Lancet*. 2022;399(10326):729-740.
2. Cheung G et al. Presented at the 22nd European Society of Retina Specialists Congress, Hamburg, Germany, 1–4 September, 2022.
3. Karampelas M et al. *Ophthalmol Ther*. 2020;9(4):739-756.
4. Freeman WR et al. *Retina*. 2011;31(9):1812-1818.
5. Schmidt-Erfurth U et al. *Ophthalmology*. 2015;122(4):822-832.

## Results

### 1. Most Patients in TENAYA/LUCERNE had a PED Involving the Foveal Centre at Baseline

**TENAYA/LUCERNE Pooled: Post Hoc Analysis**

In TENAYA/LUCERNE, PED was defined as an RPE elevation with a **width of ≥ 350 µm**

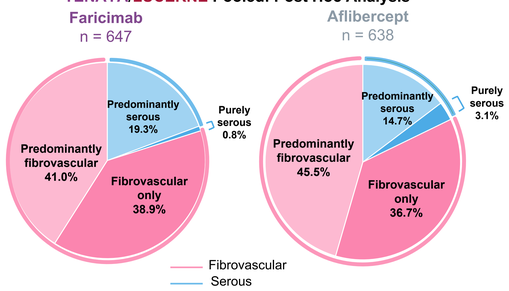
| | Faricimab Up to Q16W N = 665 | Aflibercept Q8W N = 664 |
|---|---|---|
| **Presence of PED[a], n (%)** | n = 664 | n = 663 |
| PED at any location | 647 (97.4) | 638 (96.2) |
| PED in centre 1 mm | 604 (91.0) | 606 (91.4) |
| PED at foveal centre | 486 (73.2) | 469 (70.7) |
| **Maximum thickness of PED[b], µm** | n = 656 | n = 660 |
| Mean (SE) | 252.9 (7.4) | 239.8 (7.2) |
| Median (Q1–Q3) | 185.0 (126.5–316.0) | 176.5 (125.0–300.5) |

**PED thickness** at baseline was **balanced** across treatment arms

[a] Percentages are based on the number of patients with PED type non-missing at baseline. [b] As measured within the 6-mm ETDRS grid. Max PED was based on patients who had max PED thickness > 0 µm. Patients with measurements of 0 were excluded from the analysis. ETDRS, Early Treatment Diabetic Retinopathy Study; PED, pigment epithelial detachment; Q, Quarter; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium; SE, standard error.

### 2. Among Eyes With PED in Any Location, ~20% of PEDs at Baseline Were Serous

**TENAYA/LUCERNE Pooled: Post Hoc Analysis**




PED, pigment epithelial detachment.

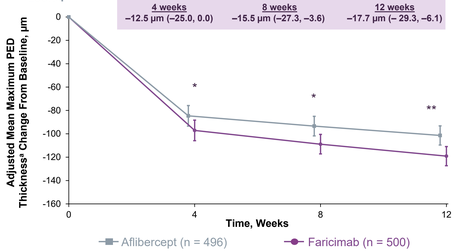
### 3. Greater Reduction in Maximum PED Thickness With Faricimab vs Aflibercept in the H2H Dosing Phase

**In Eyes With Presence of PED ≥ 125 µm at Baseline**

Baseline mean
303.9 µm
290.3 µm

**Difference vs aflibercept**
Adjusted mean thickness at each time point (95% CI):

| 4 weeks | 8 weeks | 12 weeks |
|---|---|---|
| −12.5 µm (−25.0, 0.0) | −15.5 µm (−27.3, −3.6) | −17.7 µm (−29.3, −6.1) |

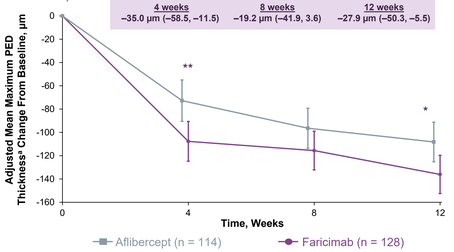



**In Eyes With Presence of Serous PED at Baseline**

Baseline mean
462.8 µm
432.1 µm

**Difference vs aflibercept**
Adjusted mean thickness at each time point (95% CI):

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

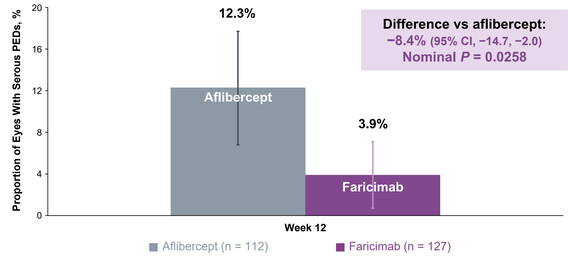



* Nominal $P < 0.05$ vs aflibercept; ** Nominal $P < 0.01$ vs aflibercept. $P$ values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the $P$ values. [a] Within the 6-mm ETDRS grid. PED thickness results are based on a mixed model for repeated measures 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 centre (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; 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.

### 4. Fewer Eyes Had Presence of Serous PEDs With Faricimab vs Aflibercept at Week 12[a]

**TENAYA/LUCERNE Pooled: Post Hoc Analysis**

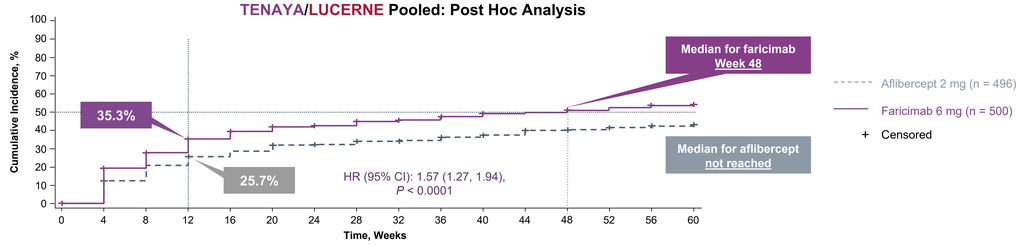
**Difference vs aflibercept:**
**−8.4% (95% CI, −14.7, −2.0)**
**Nominal $P = 0.0258$**




[a] In eyes with presence of serous PED at baseline. Predominantly serous and serous PEDs are reported as serous PED. CMH-weighted estimates are reported. These are based on CMH test stratified by baseline BCVA (≥ 74, 73–55 and ≤ 54 letters), baseline LLD (< 33, ≥ 33 letters), region (United States and Canada vs the rest of the world) and study (TENAYA vs LUCERNE). Nominal $P$ value is obtained with CMH test for superiority. $P$ values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the $P$ values. 95% CIs are shown. BCVA, best-corrected visual acuity; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; LLD, low-luminance deficit; PED, pigment epithelial detachment.

### 5. Time to First Reduction of Maximum PED Thickness by 50% From Baseline Was Faster With Faricimab Than Aflibercept[a]

**TENAYA/LUCERNE Pooled: Post Hoc Analysis**




| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aflibercept 2 mg | 496 | 493 | 429 | 387 | 362 | 348 | 324 | 322 | 310 | 301 | 277 | 267 | 255 | 253 | 245 | 231 |
| Faricimab 6 mg | 500 | 498 | 401 | 357 | 317 | 294 | 278 | 272 | 259 | 248 | 234 | 219 | 218 | 208 | 202 | 193 |

[a] In eyes with presence of PED ≥ 125 µm at baseline. Event is defined as first reduction in PED w/n 6-mm ETDRS grid by 50% from baseline. Summaries of time to first reduction in PED w/n 6-mm ETDRS grid by 50% from baseline are Kaplan–Meier estimates, with the time variable defined as the target visit week. Patients with missing PED 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. Results from stratified analyses are presented for HR and log-rank test. Stratification factors are baseline PED type (fibrovascular vs serous), baseline BCVA (≥ 74, 73–55 and ≤ 54 letters), baseline low-luminance deficit (< 33, ≥ 33 letters), region (United States and Canada, Asia and the rest of the world), reading centre (Vienna vs Duke) and study (GR40306 vs GR40844). HRs were estimated by Cox regression. An HR > 1 favours faricimab over aflibercept. CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; HR, hazard ratio; PED, pigment epithelial detachment.

### 6. Safety

- Faricimab was well tolerated with a safety profile comparable with aflibercept
- There was a higher number of RPE tears with faricimab (2.9%) compared with aflibercept (1.5%)
- This difference was not clinically or statistically significant. Most of the events were non-serious, mild, reported as not related to study drug and did not result in sustained vision loss
- Generally, RPE tears were associated with larger baseline PED heights and most frequently occurred after 1–3 anti-VEGF injections