Relative Effectiveness of Faricimab vs Aflibercept 8 mg after Loading Phase in Neovascular Age-Related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME)

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Introduction

- New treatment options using different approaches for neovascular age-related macular degeneration (nAMD) and Diabetic Macular Edema (DME) are emerging.
- Faricimab is the first bispecific antibody targeting both, ANG-2 and VEGF-A, and was investigated in the TENAYA & LUCERNE (nAMD) as well as the YOSEMITE & RHINE (DME) trials[1]. It is approved by EMA and FDA and has quickly established itself in clinical practice.
- Subsequently, aflibercept, targeting only the VEGF pathway, was investigated at a higher dosage (8 mg vs. 2 mg) in the PULSAR & CANDELA (nAMD) as well as PHOTON (DME) trials[2].
- This research aims at investigating the relative effectiveness of faricimab vs. aflibercept 8 mg. We specifically look at the outcomes after the loading phase when both treatments were given monthly to exclude the effect of dosing related differences as both treatments were given in flexible regimens thereafter.

Methods

- A targeted literature review was conducted to identify randomized clinical trials using aflibercept 8 mg in nAMD and DME (aflibercept 2 mg was also included).
- The main outcome of interest was change in best corrected visual acuity (BCVA) and central subfield thickness (CST) from baseline until the end of the loading phase (12 weeks).
- Seven studies with relevant data were eligible informing a Bayesian Network Meta-Analysis (NMA) to estimate the efficacy of faricimab vs. aflibercept 8 mg.
- Differences, prediction intervals and the probability of faricimab leading to better outcomes were calculated using random-effects (RE) and fixed-effect (FE) models and for nAMD and DME separately as well as pooled together.
- The analysis used Bayesian methods to control for between study heterogeneity, which was informed by NMAs comparing faricimab and other monotherapies submitted to NICE[3] and CADTH[4] in nAMD, and recently published for DME[5].

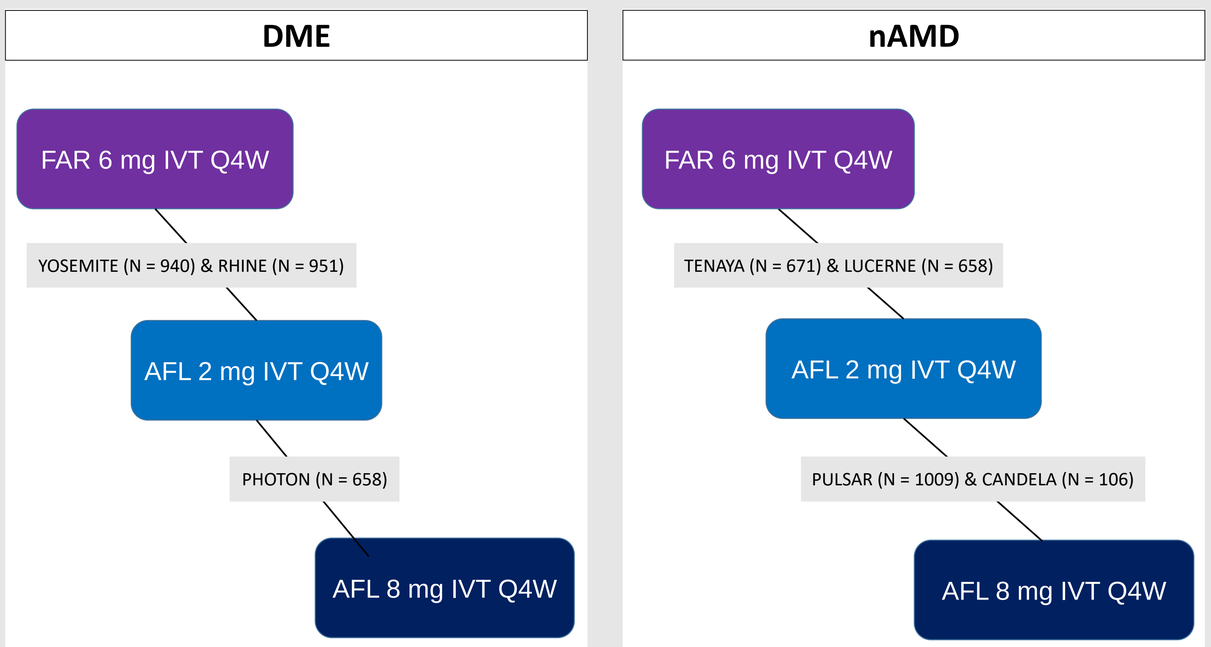
Results

- Baseline characteristics including BCVA were broadly similar between the included studies, suggesting no important differences in known confounding factors that may lead to bias. (figure 2).
- Using the random effects model, the mean change in BCVA at 12 weeks was numerically greater for faricimab vs. aflibercept 8 mg across all analyses. Point estimates ranged between 1-2 letters. (figure 3)
- The mean change in CST was statistically greater with faricimab vs aflibercept 8 mg in DME and in the pooled analysis, and numerically greater in nAMD. Point estimates ranged between 15 – 22 microns. (figure 4)
- Prediction intervals using the random effects model consistently showed statistically better results for CST and numerically better visual acuity estimates for faricimab vs. aflibercept 8 mg. (figure 5)
- The associated probability of faricimab showing better vision outcomes than aflibercept 8 mg in both indications was 77% or higher. The associated probability of faricimab showing better retinal drying than aflibercept 8 mg was 93% or higher in both indications. (figure 6)
- Fixed effects results were consistent across all analysis.

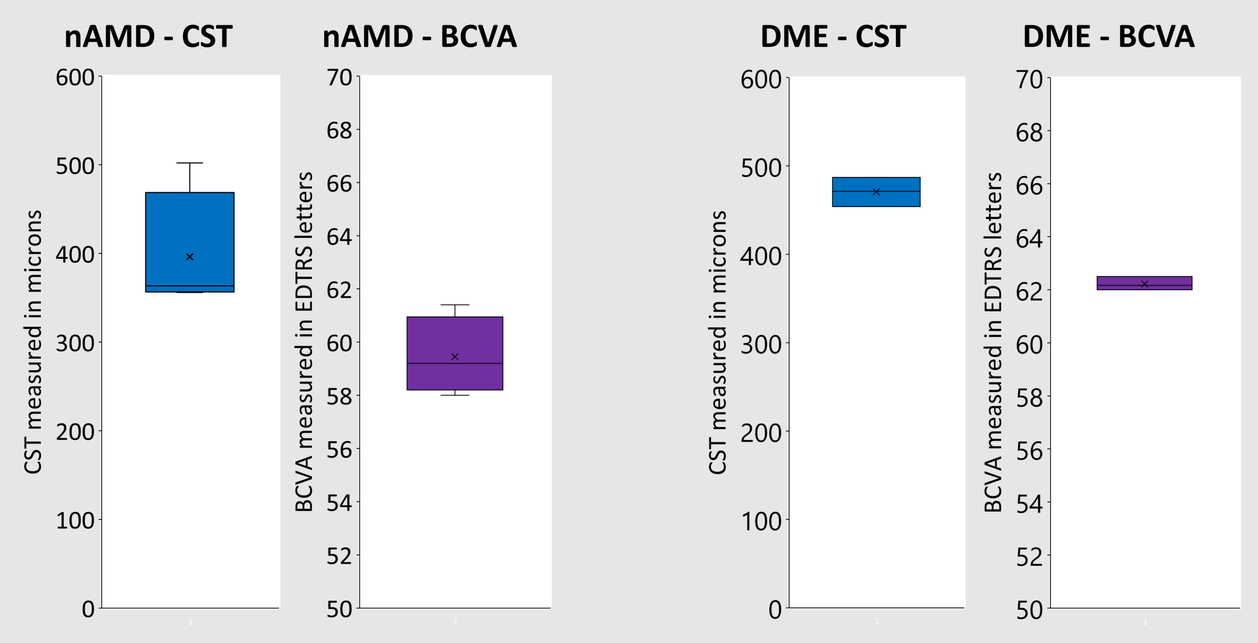
Conclusions

- The results indicate that there is a high probability that faricimab is associated with a better retinal drying profile than aflibercept given at the standard dose of 2 mg as well as a higher dose of 8 mg, although credible intervals are crossing zero in some analysis. At the same time faricimab is associated with similar or numerically better vision outcomes.
- Retinal fluid is a key factor in patients ability to extend treatment intervals. Based on the findings presented here, faricimab offers the potential to noticeably reduce the significant treatment burden for patients, caregivers, and physicians.
- Results suggest that faricimab may help reduce capacity challenges that many health systems are facing given the increasing prevalence of nAMD and DME to a greater extent than aflibercept 2 mg or 8 mg.

1. Network of Evidence Comparing Faricimab vs. Aflibercept

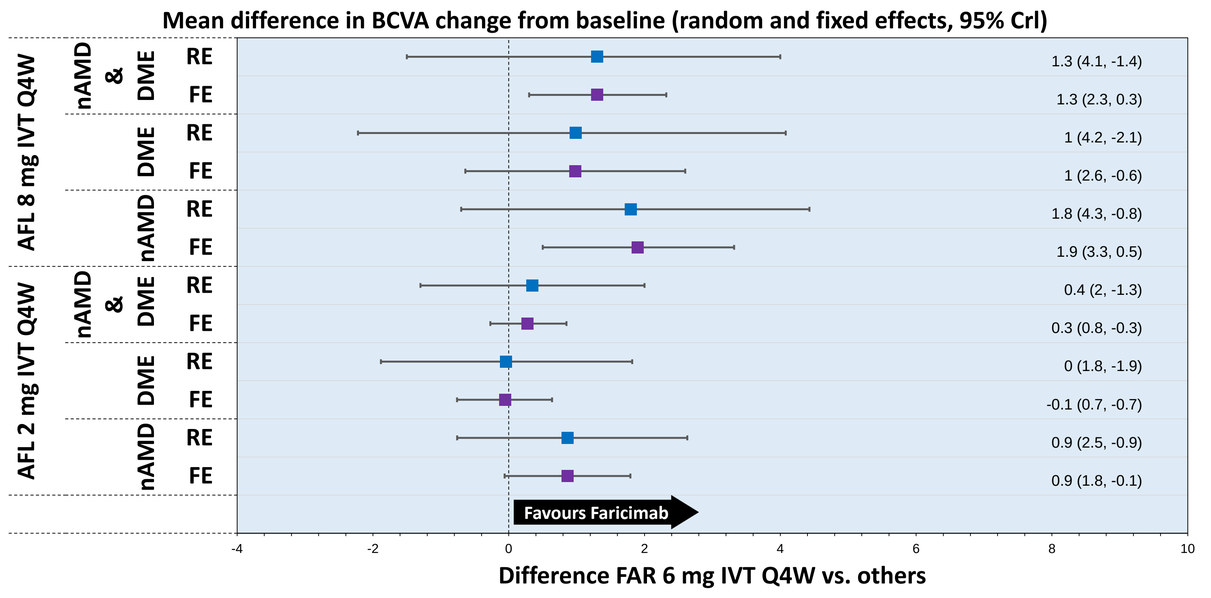


2. Baseline Characteristics of Included Studies



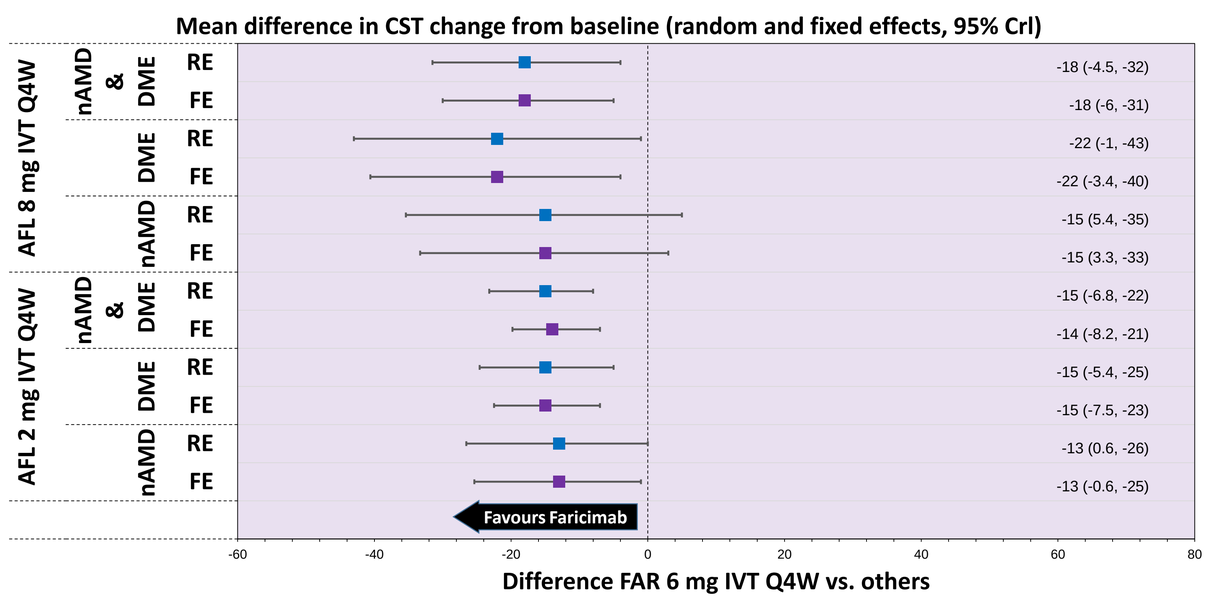
Whisker plots present the first and third quartile and the 95% Confidence interval. The outlier in nAMD is CANDELA with a small sample size.

3. Forest Plot of Differences and 95% Credible Intervals of Faricimab vs. Aflibercept: Mean Difference in BCVA Change From Baseline At 12 Weeks



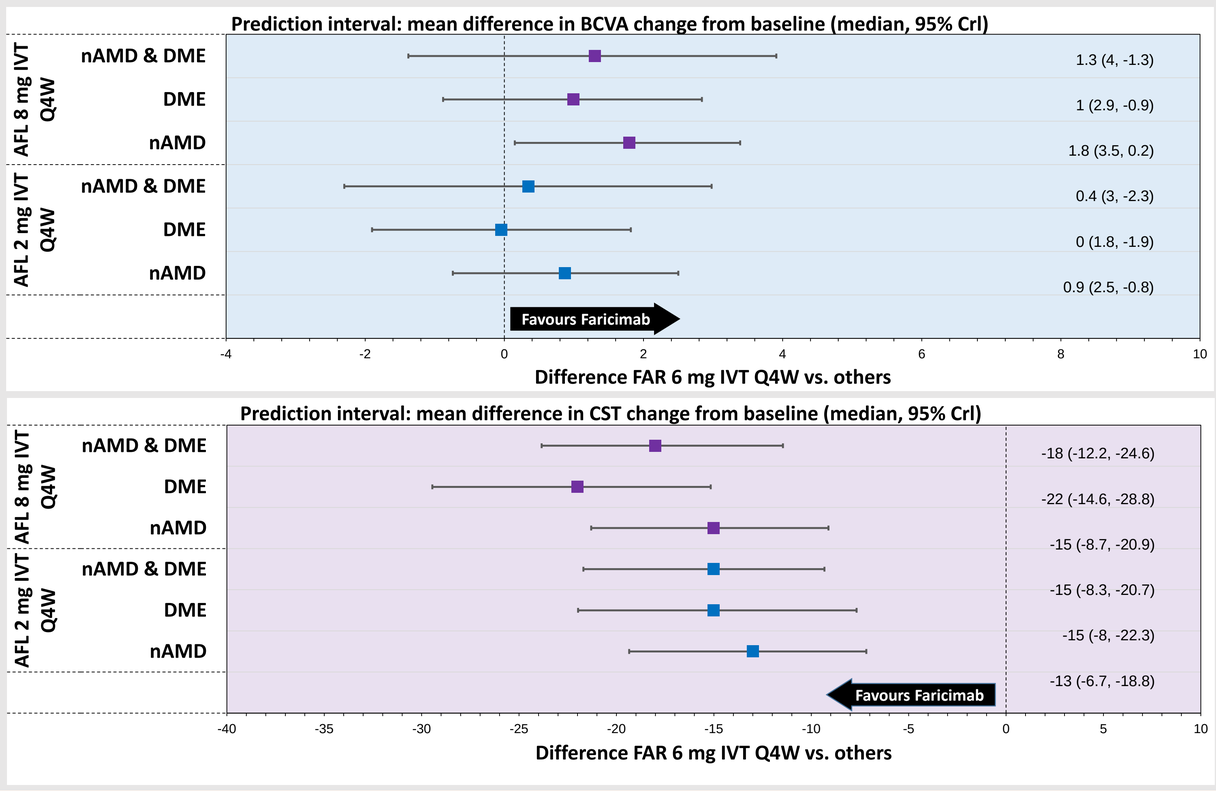
At the 12-week time point, the mean change in BCVA was numerically greater or similar for faricimab across all analysis vs. all formulations of aflibercept. The magnitude of the treatment effect ranged from no difference to a two letter improvement.

4. Forest Plot of Differences and 95% Credible Intervals of Faricimab vs. Aflibercept: Mean Difference in CST Change From Baseline At 12 Weeks

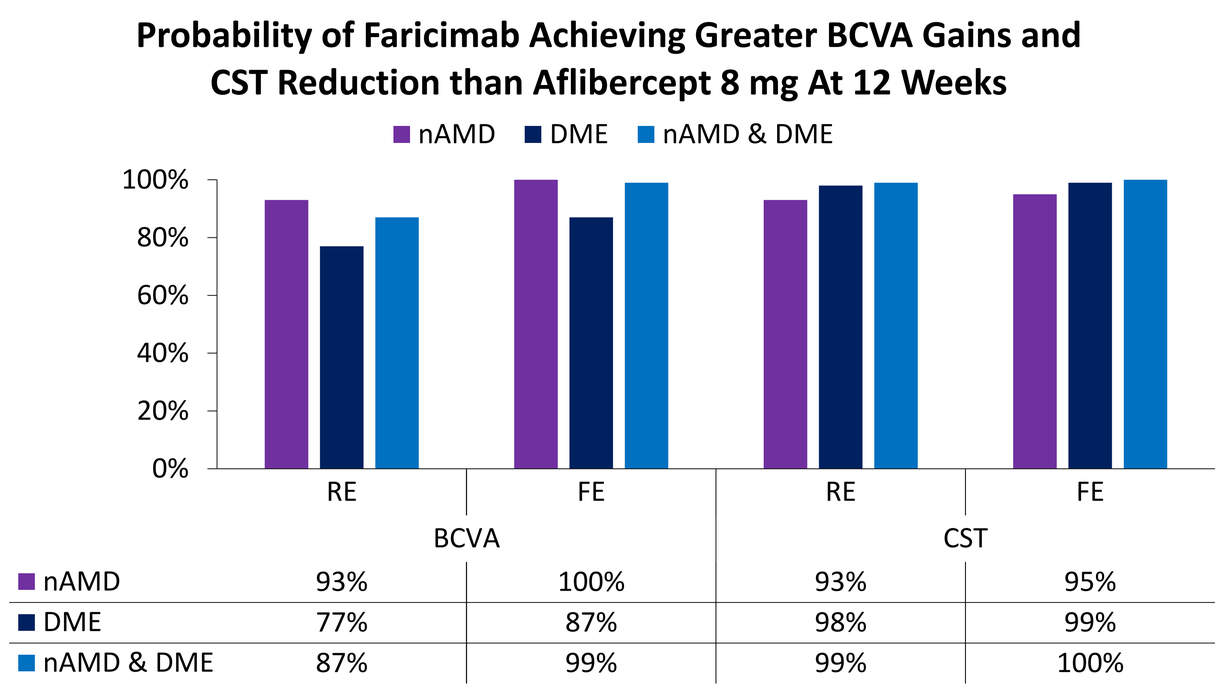


The mean change in CST was statistically greater with faricimab in DME and the pooled analysis as well as numerically greater in nAMD vs. all formulations of aflibercept. The magnitude of the treatment effect ranged from 13 – 22 microns and was consistent across all analysis.

5. Forest Plot of Prediction Intervals for Differences in BCVA and CST At 12 Weeks Using the Random Effects Model



6. Probability of Faricimab Achieving Greater BCVA Gains and Greater CST Reduction than Aflibercept 8 mg At 12 Weeks



	BCVA RE	BCVA FE	CST RE	CST FE
nAMD	93%	100%	93%	95%
DME	77%	87%	98%	99%
nAMD & DME	87%	99%	99%	100%

References

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Efficacy , durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised , double masked, phase 3 trials; Wykoff , Charles CAaberg , Thomas et al.; The Lancet, Volume 399, Issue 10326, 741 755; DOI: 10.1016/S0140 6736(22)00018 6.
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Financial Disclosures

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