Network Meta-Analyses of Number of Injections With Aflibercept 8 mg Versus Faricimab in nAMD and DME

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Disclosures

- Theodore Leng has received funding from Astellas and served as a consultant for Astellas, Boehringer Ingelheim, Regeneron Pharmaceuticals, Inc., Roche/Genentech, Topcon, and Virtual Field
- Andreas Kuznik, Yingxin Xu, and Steven Sherman are employees and stockholders of Regeneron Pharmaceuticals, Inc.
- Ali Mojebi, Sam Keeping, and Keith Chan are employees of Precision AQ, which received funding from Regeneron Pharmaceuticals, Inc., for conducting this analysis
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Objectives

- Reducing the frequency of intravitreal injections while maintaining efficacy is a key goal in reducing the treatment burden associated with anti-VEGF therapy for patients with DME and nAMD
- Newer agents are available that allow for longer intervals between injections without compromising efficacy, including:
  - Aflibercept 8 mg, a novel high-dose formulation anti-VEGF agent that delivers a 4-fold higher molar dose than aflibercept 2 mg[1,2]
  - Faricimab 6 mg, a dual angiopoietin-2 and VEGF-A inhibitor[3-6]

A network meta-analysis was performed to indirectly compare relative numbers of injections and efficacy between aflibercept 8 mg and faricimab treat-and-extend in patients with DME or nAMD

DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

1. Brown DM et al. *Lancet*. 2024;403:1153–1163. 2. Lanzetta P et al. *Lancet*. 2024;403:1141–1152. 3. Wykoff CC et al. *Lancet*. 2022;399:741–755. 4. Wong TY et al. *Ophthalmology*. 2024;131:708–723. 5. Heier JS et al. *Lancet*. 2022;399:729–740. 6. Khanani AM et al. *Ophthalmology*. 2024;131:914–926.

Methods

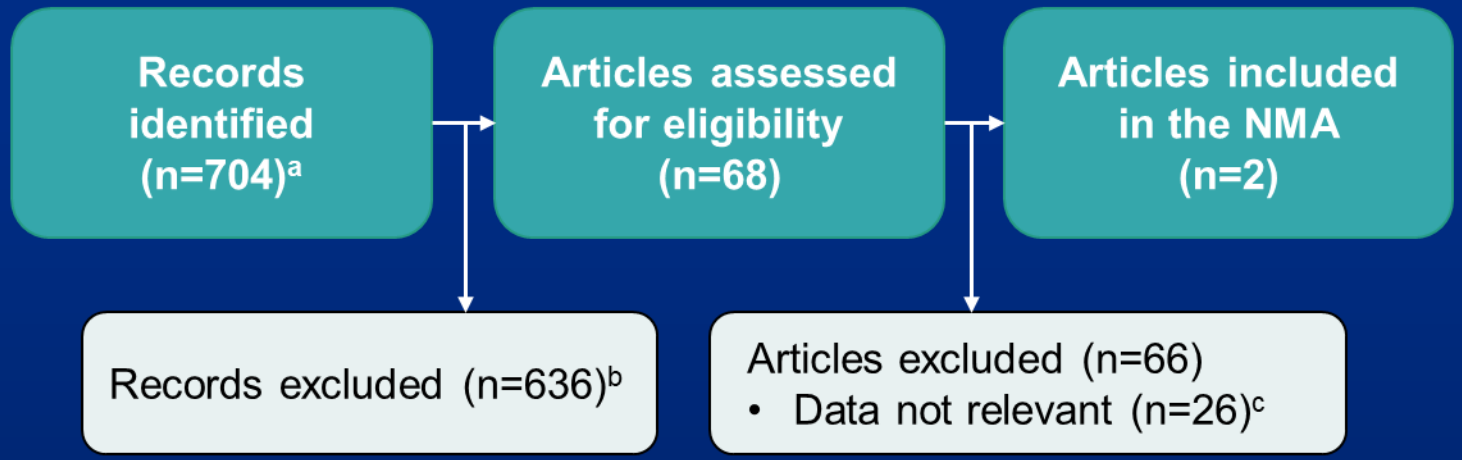
- A systematic literature review was performed to identify published manuscripts reporting data for RCTs with two-year observation periods that evaluated aflibercept 8 mg or faricimab treat-and-extend (6 mg) in DME or nAMD
  - For aflibercept 8 mg RCTs where only 1-year data had been reported, 2-year data were extracted from corresponding clinical study reports
- Outcomes included injection frequency, absolute change from baseline in BCVA, absolute change from baseline in CST, and percentage change from baseline in CST
- Fixed-effect network meta-analyses were performed within Bayesian statistical models in accordance with National Institute for Health and Care Excellence[1] and International Society for Pharmacoeconomics and Outcomes Research[2] guidelines using R statistical software[3]
  - Data for the patients who received aflibercept 8 mg every 12 weeks or every 16 weeks were pooled to create a single aflibercept 8-mg treatment group
  - Results were reported as mean differences with 95% credible intervals
  - $P<0.05$ denoted statistical significance

BCVA, best-corrected visual acuity; CST, central subfield thickness; RCT, randomized controlled trial.

1. Dias S et al. *Med Decis Making*. 2013;33:607–617. 2. Hoaglin DC et al. *Value Health*. 2011;14:429–437. 3. R: A language and environment for statistical computing (v4.4.1) [https://www.r-project.org].

Study Selection

- Two articles reporting two-year data for the YOSEMITE/RHINE (DME)[1] and TENAYA/LUCERNE (nAMD)[2] RCTs of faricimab treat-and-extend versus aflibercept 2 mg were included from the systematic literature review

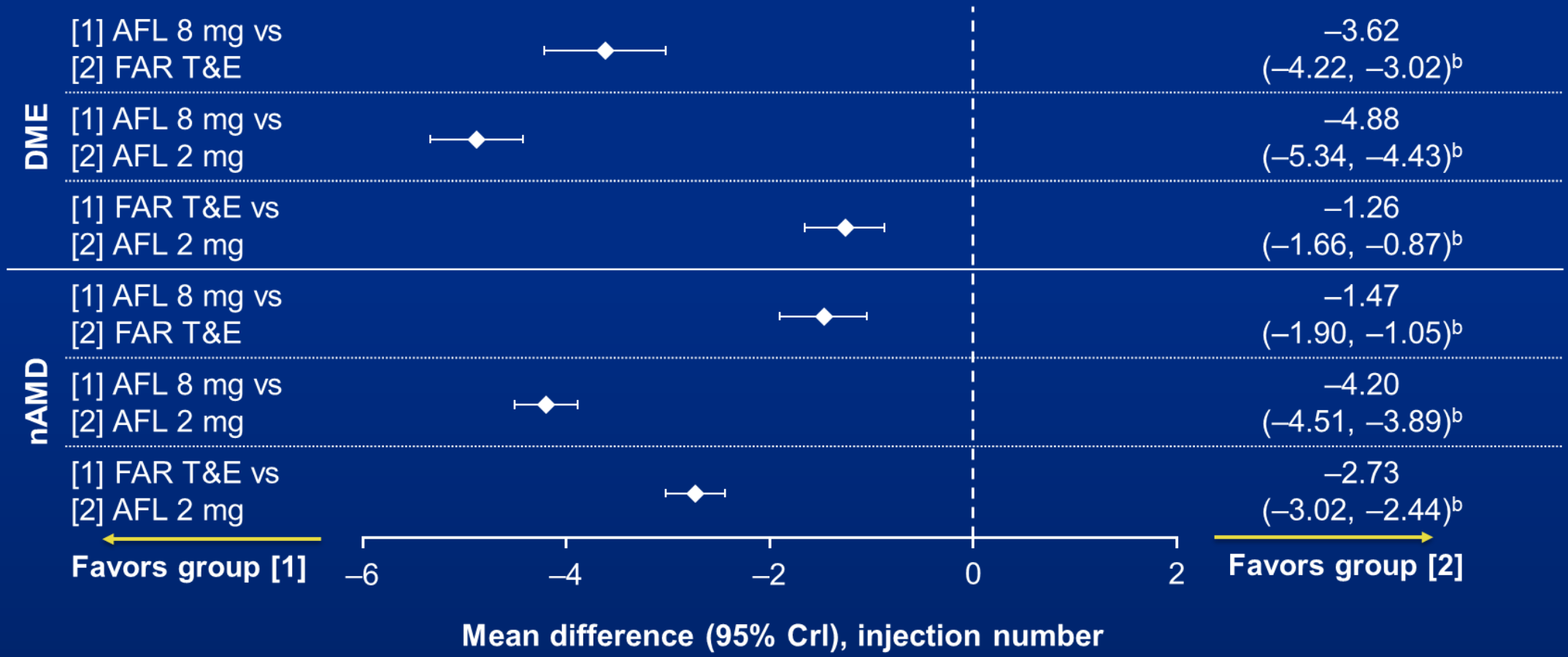


- Two-year data for the PHOTON (DME)[3] and PULSAR (nAMD)[4] RCTs of aflibercept 8 mg versus aflibercept 2 mg were obtained from clinical study reports

[a]MEDLINE/Embase. [b]Including 2 duplicates. [c]Articles that met broad SLR eligibility criteria but were not relevant to the NMA (reported data for RCTs that evaluated aflibercept 2 mg vs an anti-VEGF agent other than either faricimab or aflibercept 8 mg, subgroup or secondary analyses, or reported 1-year data only). NMA, network meta-analyses.

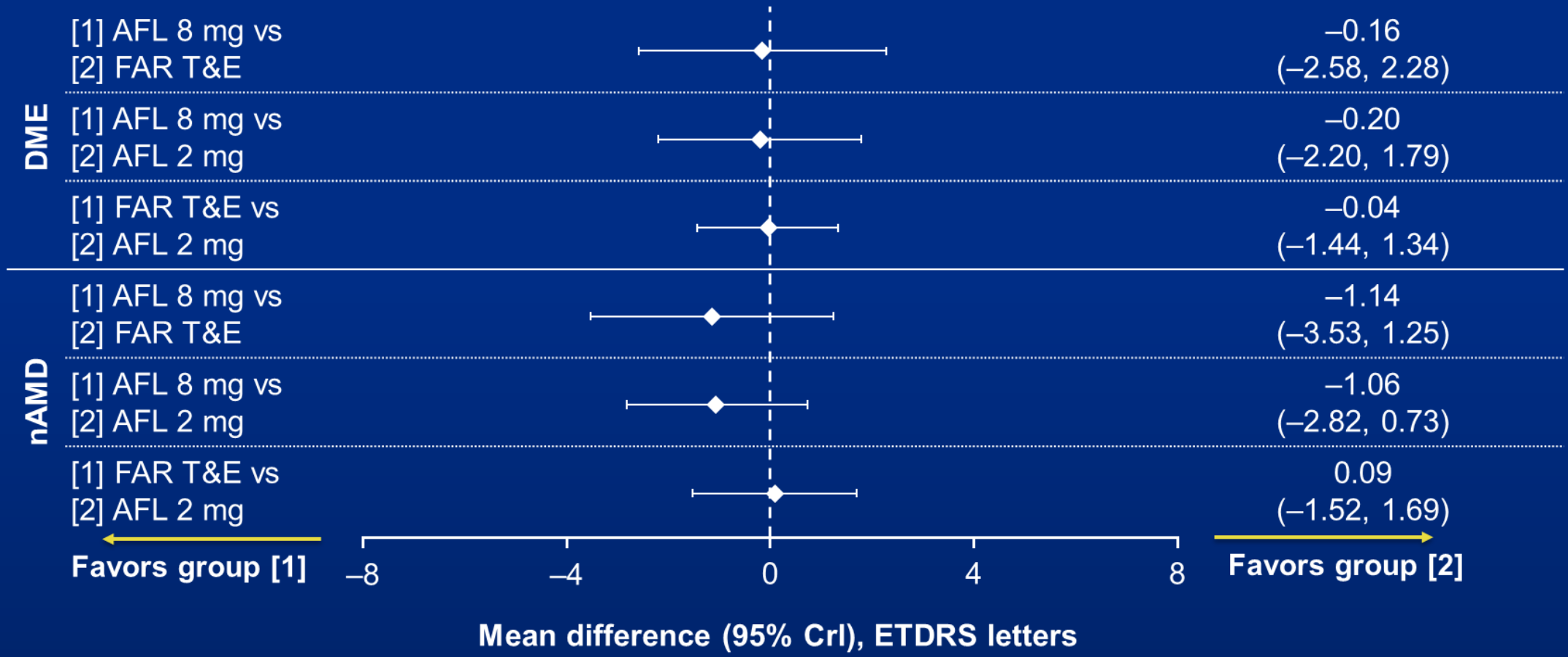
1. Wong TY et al. *Ophthalmology*. 2024;131: 708–723. 2. Khanani AM et al. *Ophthalmology*. 2024;131:914–926. 3. PHOTON clinical study report (data on file). 4. PULSAR clinical study report (data on file).

Mean Difference in Number of Injections Between Treatments at 2 Years[a]



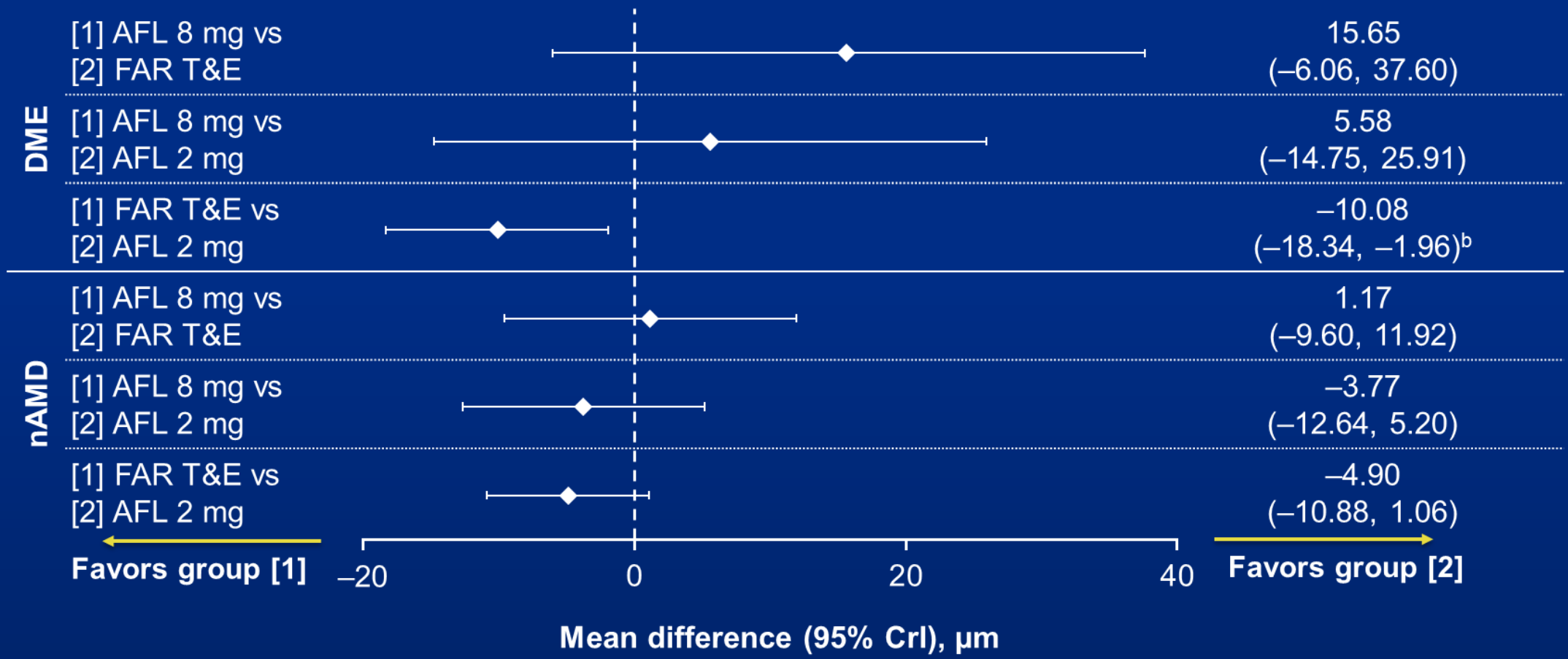
Group [1] and [2] refer to the first and second group in each pair of comparisons, e.g., AFL 8 mg (group [1]) vs FAR T&E (group [2]).
[a]To account for varying RCT durations, mean numbers of injections were adjusted to 104 weeks across RCTs. [b]$P<0.05$.
AFL, aflibercept; CrI, credible interval; FAR, faricimab; T&E, treat-and-extend.

Mean Difference in Absolute Change in BCVA Between Treatments at 2 Years[a]



Group [1] and [2] refer to the first and second group in each pair of comparisons, e.g., AFL 8 mg (group [1]) vs FAR T&E (group [2]).
[a]Defined as Week 96 in PHOTON and PULSAR, the average of Weeks 92, 96, and 100 in YOSEMITE/RHINE, and the average of Weeks 104, 108, and 112 in TENAYA/LUCERNE.
ETDRS, Early Treatment Diabetic Retinopathy Study.

Mean Difference in Absolute Change in CST Between Treatments at 2 Years[a]



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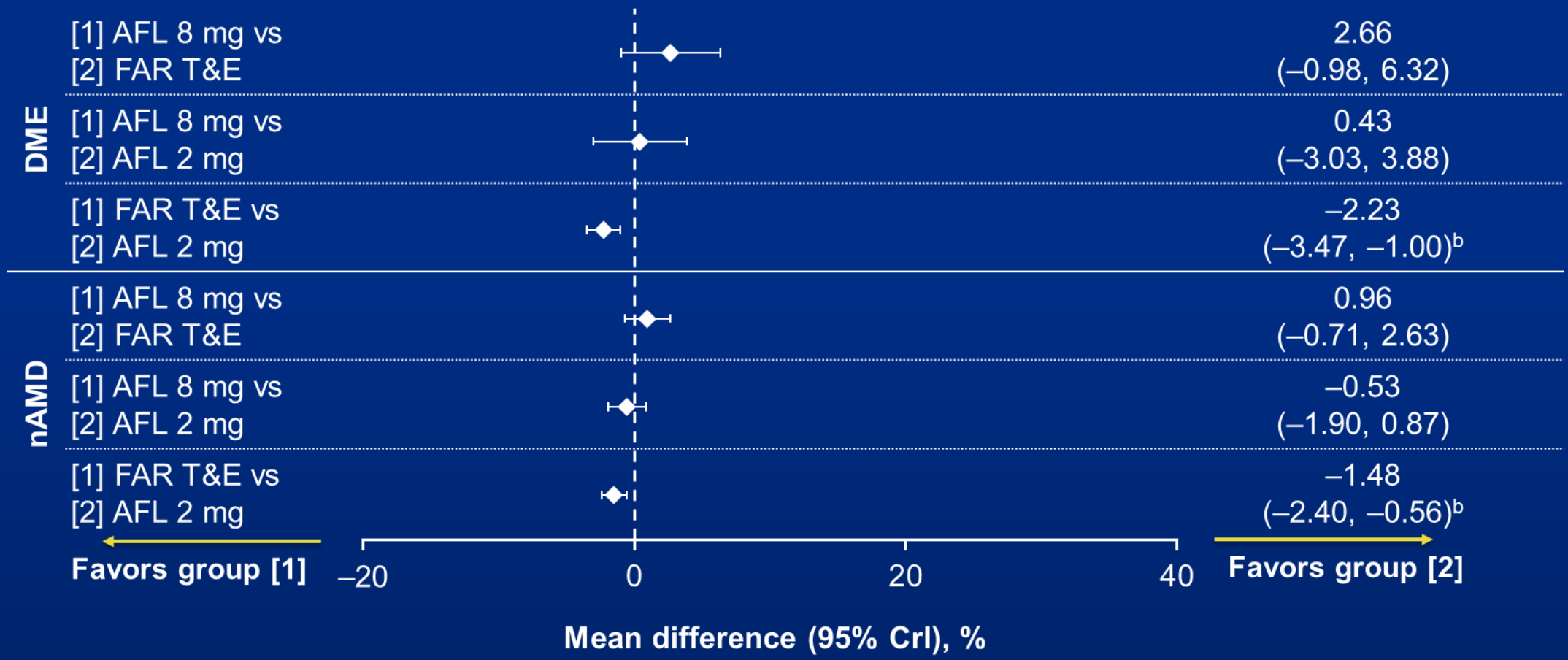
[b]$P<0.05$.

Mean Difference in Percentage Change in CST Between Treatments at 2 Years[a]



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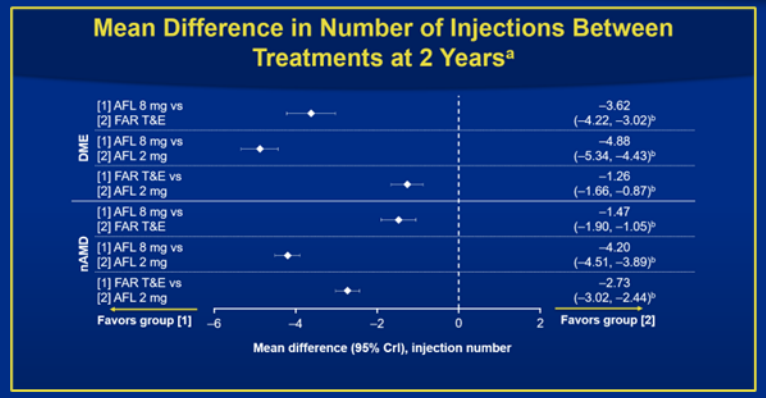
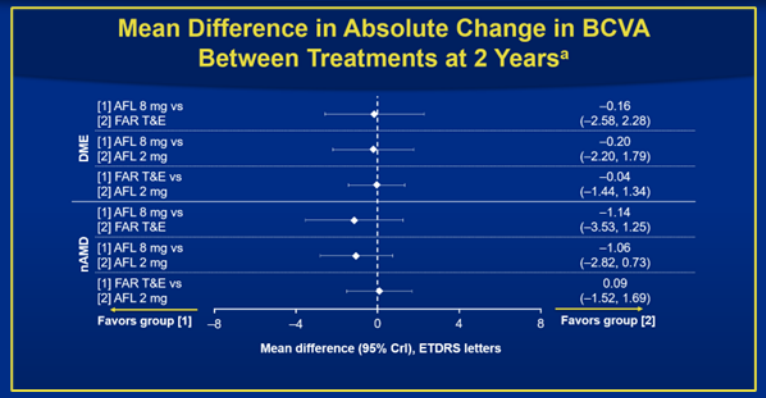
[a]Defined as Week 96 in PHOTON and PULSAR, the average of Weeks 92, 96, and 100 in YOSEMITE/RHINE, and the average of Weeks 104, 108, and 112 in TENAYA/LUCERNE.
[b]$P<0.05$.

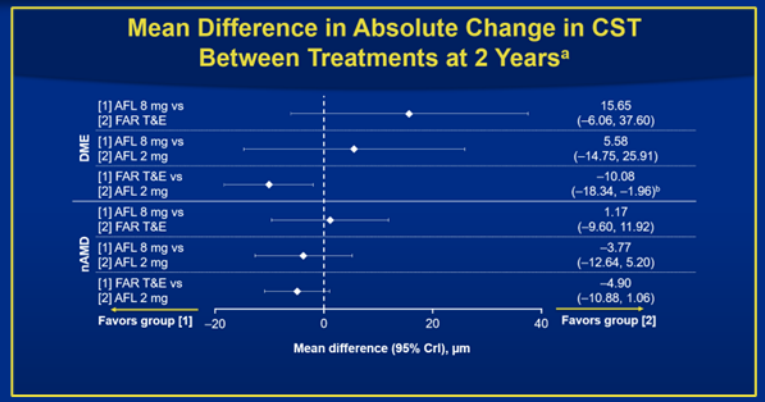
Limitations

- Lack of randomization between groups being compared
- Differences in clinical trial designs (e.g., eligibility criteria, protocol-defined injection numbers, dosing interval modification criteria, durations of follow-up, and CST reporting)
  - As baseline CST values were imbalanced across the RCTs, and baseline CST values influence absolute changes in CST from baseline, interpretation of the result for difference in absolute change in CST should be made with caution
  - Percentage changes in CST were also calculated; however, as this outcome was not reported for all trials, some assumptions were made, and the results should also be interpretated with caution

Conclusions







- Despite inherent limitations, network meta-analyses allow for the comparison of treatments that may not have been directly evaluated in head-to-head clinical trials, when conducted appropriately
- This network meta-analysis showed that aflibercept 8 mg was associated with significantly fewer intravitreal injections over 2 years compared with faricimab treat-and-extend in patients with DME and nAMD, while offering comparable efficacy
- Aflibercept 8 mg may help reduce the burden associated with anti-VEGF therapy and improve long-term visual outcomes