Network Meta-Analyses of Number of Injections With High-Dose Aflibercept Versus Faricimab in Patients With Diabetic Macular Edema and Neovascular Age-Related Macular Degeneration

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BACKGROUND & PURPOSE

- Reducing the frequency of intravitreal injections while maintaining efficacy is a key goal in reducing the treatment burden associated with anti-vascular endothelial growth factor (VEGF) therapy for patients with diabetic macular edema (DME) and neovascular age-related macular degeneration (nAMD)
- Newer anti-VEGF agents with prolonged VEGF suppression allow for longer intervals between injections without compromising efficacy, including:
  - Aflibercept (AFL) 8 mg, a novel high-dose formulation that delivers a 4-fold higher molar dose than AFL 2 mg[1,2]
  - Faricimab (FAR) 6 mg, a dual angiopoietin-2 and VEGF-A inhibitor[3-6]
- A network meta-analysis (NMA) was performed to indirectly compare relative numbers of injections and efficacy between AFL 8 mg and FAR treat-and-extend (T&E) in patients with DME or nAMD

METHODS

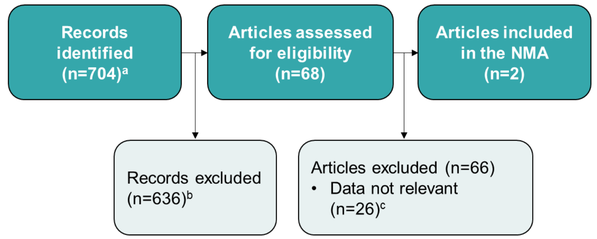
- A systematic literature review (SLR) was performed to identify randomized controlled trials (RCTs) with 2-year observation periods that evaluated AFL 8 mg or FAR T&E (6 mg) in patients with DME or nAMD
  - For RCTs of AFL 8 mg that reported 1-year data only, 2-year data were extracted from corresponding Clinical Study Reports where available
- Outcomes included injection frequency, absolute change from baseline in best-corrected visual acuity (BCVA), absolute change from baseline in central retinal/subfield thickness (CRT/CST), and percentage change from baseline in CRT/CST
- Fixed-effect NMAs were performed within Bayesian statistical models in accordance with National Institute for Health and Care Excellence[7] and International Society for Pharmacoeconomics and Outcomes Research[8] guidelines using R statistical software[9]
  - For the purposes of this analysis, patients receiving AFL 8 mg every 12 weeks (8q12) or every 16 weeks (8q16) were pooled to create a single AFL 8-mg treatment group
- Results were reported as mean differences with 95% credible intervals (CrIs)
  - $P<0.05$ denotes statistical significance

RESULTS

Study Selection

- Two-year data for the PHOTON (DME)[10] and PULSAR (nAMD)[11] RCTs identified in the SLR were obtained from Clinical Study Reports
  - These RCTs compared 8q12 or 8q16 following 3 initial monthly injections with AFL 2 mg every 8 weeks (2q8) following 5 (PHOTON)[10] or 3 (PULSAR)[11] initial monthly injections
  - In the AFL 8-mg groups, injection intervals could be shortened to every 8 weeks from Week 16, or extended to every 24 weeks from Week 52, if pre-specified disease activity criteria were met[10,11]
- Two-year data for the YOSEMITE/RHINE (DME)[4] and TENAYA/LUCERNE (nAMD)[6] RCTs were obtained from articles identified in the SLR (**Figure 1**)
  - These RCTs compared FAR T&E following ≥4 initial monthly injections with AFL 2q8 following 5 (YOSEMITE/RHINE)[4] or 3 (TENAYA/LUCERNE)[6] initial monthly injections
  - In the FAR T&E groups, injection intervals could be extended to every 16 weeks if pre-specified disease activity criteria were met[4,6]

Figure 1. Summary of SLR



[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 AFL 2 mg vs an anti-VEGF agent other than either FAR or AFL 8 mg; subgroup or secondary analyses; or reported 1-year data only).

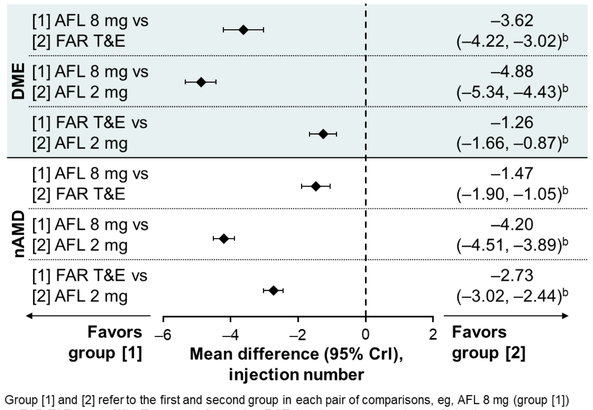
Injection Frequency

- Treatment with AFL 8 mg was associated with significantly fewer injections compared with FAR T&E in patients with DME and nAMD (**Figure 2**)

Efficacy

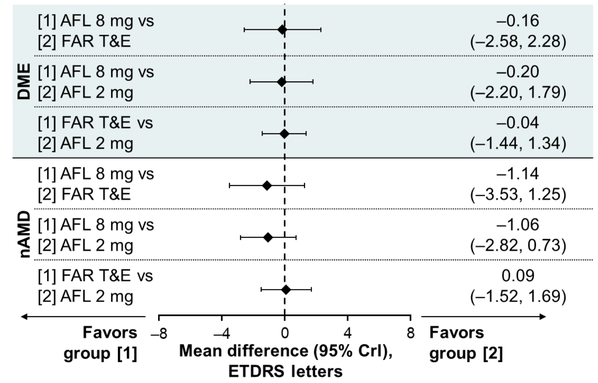
- There were no significant differences in absolute change in BCVA (**Figure 3**), absolute change in CRT/CST (**Figure 4**), or percentage change in CRT/CST (**Figure 5**), between patients treated with AFL 8 mg or FAR T&E

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



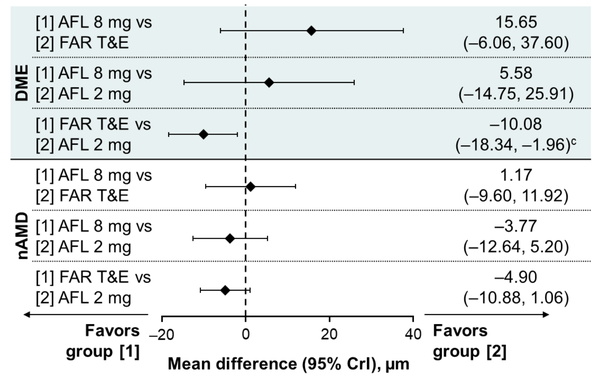
Group [1] and [2] refer to the first and second group in each pair of comparisons, eg, AFL 8 mg (group [1]) vs FAR T&E (group [2]). [a]To account for varying RCT durations, mean numbers of injections were adjusted to 104 weeks across RCTs. [b]$P<0.05$.

Figure 3. Mean Difference in Absolute Change in BCVA Between Treatments at 2 Years[a]



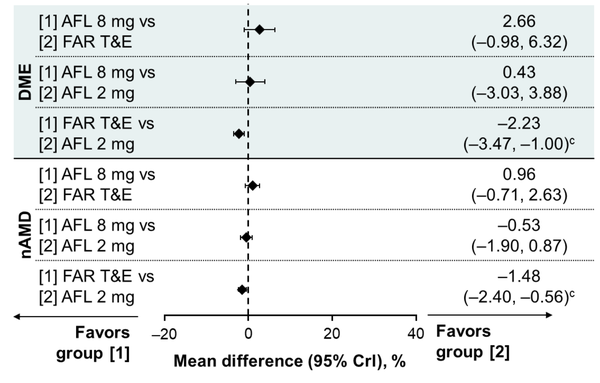
Group [1] and [2] refer to the first and second group in each pair of comparisons, eg, AFL 8 mg (group [1]) vs FAR T&E (group [2]). [a]Defined as Week 96 in PHOTON and PULSAR, the average of Weeks 92, 96, and 100 in YOSEMITE/RHINE, and the average of Weeks 104, 108, and 112 in TENAYA/LUCERNE. ETDRS,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

Figure 4. Mean Difference in Absolute Change in CRT/CST[a] Between Treatments at 2 Years[b]



Group [1] and [2] refer to the first and second group in each pair of comparisons, eg, AFL 8 mg (group [1]) vs FAR T&E (group [2]). [a]CRT (reported in PHOTON and PULSAR) and CST (reported in YOSEMITE/RHINE and TENAYA/LUCERNE) were assumed to be equivalent for the purposes of this analysis. [b]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. [c]$P<0.05$.

Figure 5. Mean Difference in Percentage Change in CRT/CST[a] Between Treatments at 2 Years[b]



Group [1] and [2] refer to the first and second group in each pair of comparisons, eg, AFL 8 mg (group [1]) vs FAR T&E (group [2]). [a]CRT (reported in PHOTON and PULSAR) and CST (reported in YOSEMITE/RHINE and TENAYA/LUCERNE) were assumed to be equivalent for the purposes of this analysis. [b]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. [c]$P<0.05$.

Limitations

- Limitations of this NMA include lack of randomization and differences in trial designs (eg, eligibility criteria, protocol-defined injection numbers, dosing interval modification criteria, follow-up durations, and CRT/CST reporting)
- As baseline CRT/CST values were imbalanced across RCTs, and baseline values influence absolute changes from baseline, interpretation of the result for difference in absolute change in CRT/CST should be made with caution

CONCLUSIONS

- Despite inherent limitations, NMAs allow for the comparison of treatments that may not have been directly evaluated in head-to-head clinical trials, when conducted appropriately
- This NMA showed that AFL 8 mg was associated with significantly fewer intravitreal injections over 2 years compared with FAR T&E in patients with DME and nAMD, while offering comparable efficacy
- AFL 8 mg may help reduce the burden associated with anti-VEGF therapy, and improve long-term visual outcomes

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Poster presented by Steven Sherman, MPH, email: steven.sherman@regeneron.com, at the ARVO 2025 Meeting, May 4-8, 2025