Systematic Review and Network Meta-Analysis of Faricimab in Neovascular Age-Related Macular Degeneration for Injection Frequency

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Introduction

- Despite great advances, current anti-VEGF treatment options for neovascular age-related macular degeneration (nAMD) require frequent injections imposing a significant burden for patients, caregivers, and physicians.
- Faricimab is a bispecific antibody targeting both, ANG-2 and VEGF. In the TENAYA and LUCERNE trials (2-year Phase III trials),[1] patients treated with individualized fixed dosing of faricimab followed by Treat & Extend (T&E) required less frequent treatments compared to aflibercept given every eight weeks (Q8W) without compromising efficacy. About 80% of patients could extend their intervals beyond Q8W.
- Clinical practice in nAMD is typically characterized by T&E as well as pro re nata (PRN) regimens. This research aims to assess the durability profile of faricimab vs. anti-VEGF treatments applied in such regimens.

Methods

- A systematic literature review was conducted to identify randomized clinical trials of anti-VEGF treatments in nAMD.
- Data on the mean number of injections after two years were extracted.
- 14 studies with relevant data were eligible informing a Bayesian Network Meta-Analysis following the NICE guidance[2] to estimate the durability of faricimab vs. other anti-VEGF treatments. Of those, 2 studies (ANCHOR and FOCUS) were comparing to Sham injections and are therefore not presented.
- Differences and the probability of faricimab requiring less frequent treatment were calculated using random-effects (RE) and fixed-effect (FE) models.
- The analysis presented were part of the faricimab reimbursement dossiers submitted to NICE and CADTH. [3,4]

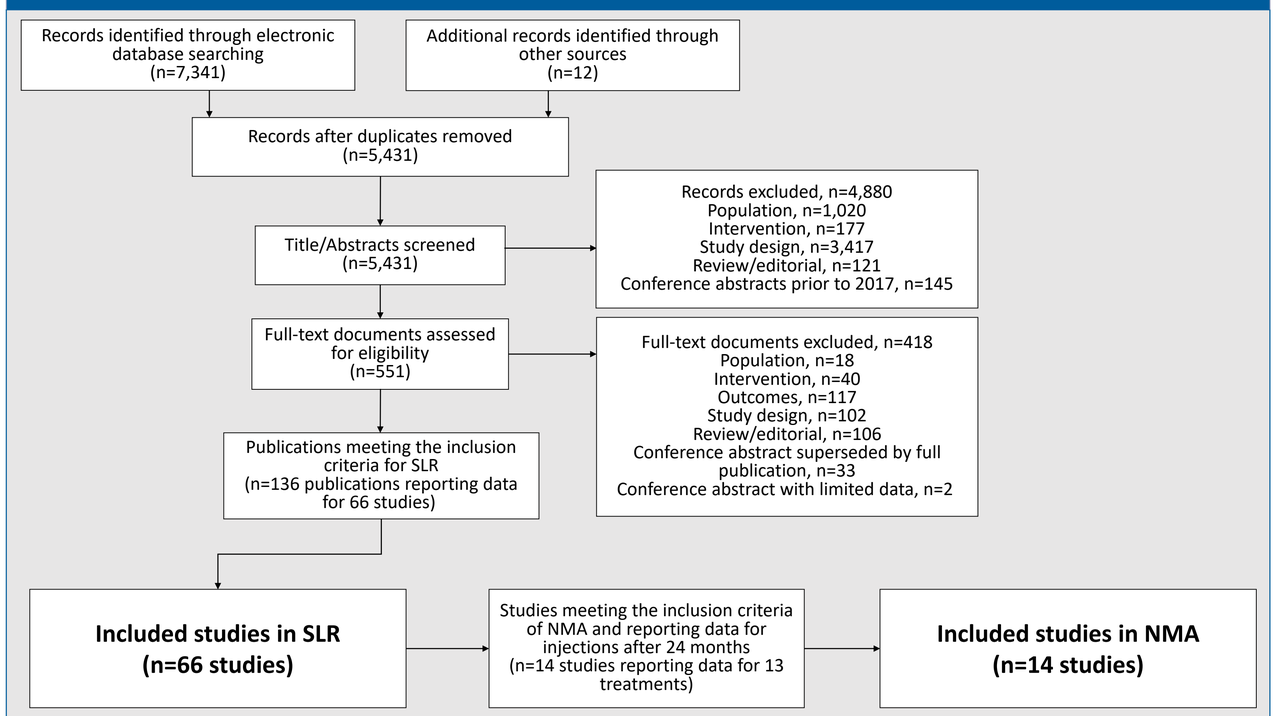
Results

- Key baseline characteristics including baseline BCVA score were similar between the included studies, suggesting no important differences in known confounding factors that may lead to bias.
- At the two year time point, the mean differences in number of injections favored faricimab vs. anti-VEGF T&E and PRN + loading regimens using a RE model which provided the best fitting model (deviance information criteria of 38.7 vs. 80.2 for FE model).
- The point estimate vs. bevacizumab, ranibizumab, aflibercept and brolucizumab applied in a T&E regimen was -6.7, -4.4, -1.8 and -1.9 respectively.
- The associated probability of faricimab requiring less frequent dosing than each comparators was 96%, 95%, 80% and 84% accordingly.
- For PRN regimens using a loading phase, a comparison was possible vs. ranibizumab with a mean difference of -3.7 and an associated probability of faricimab requiring less frequent dosing of 89%.
- Amongst the flexible treatment regimens of interest, faricimab was ranked as the best treatment with 66% probability and had the highest SUCRA score (0.89).
- FE results were consistent.

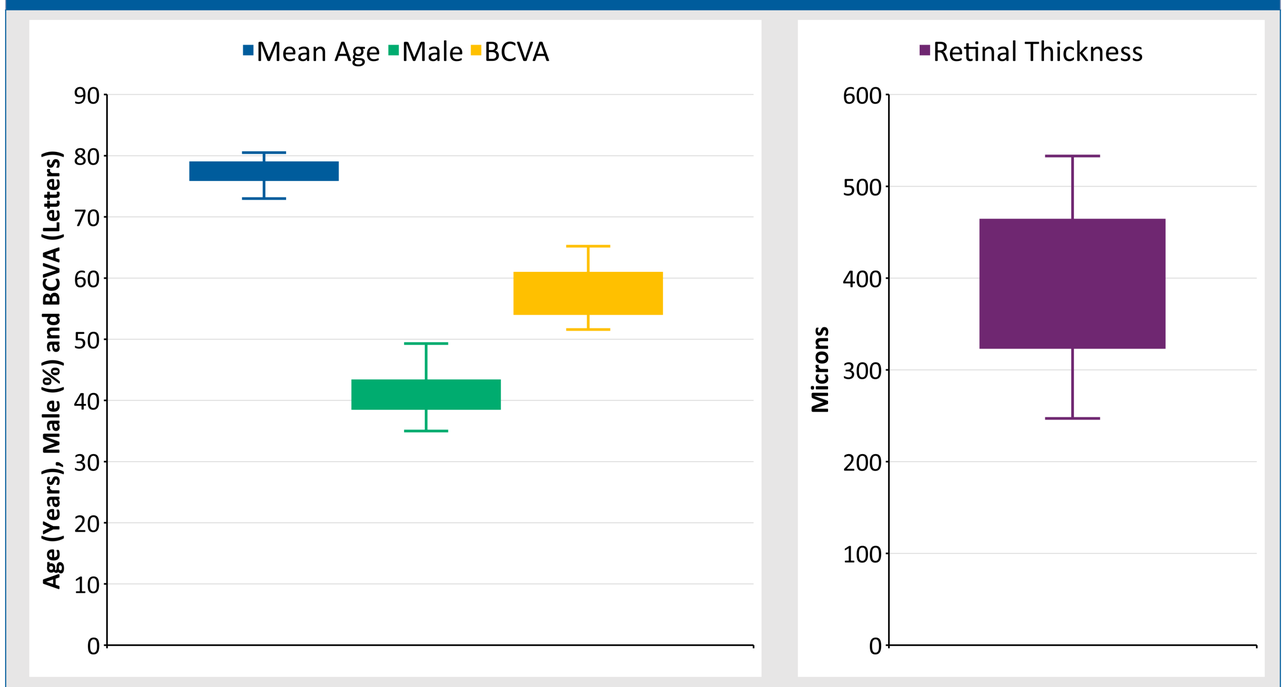
Conclusions

- Although credible intervals are crossing one, the results indicate that there is a high probability that faricimab is associated with a better durability profile than current treatment options administered in flexible regimes that are typically used in clinical practice.
- Based on these findings, faricimab offers the potential to noticeably reduce the significant treatment burden for patients, caregivers, and physicians, particularly versus ranibizumab and bevacizumab. It may also help tackling the capacity challenges that many health systems are facing given the increasing prevalence of nAMD.

1. PRISMA Flow Diagram Showing the Study Identification Process

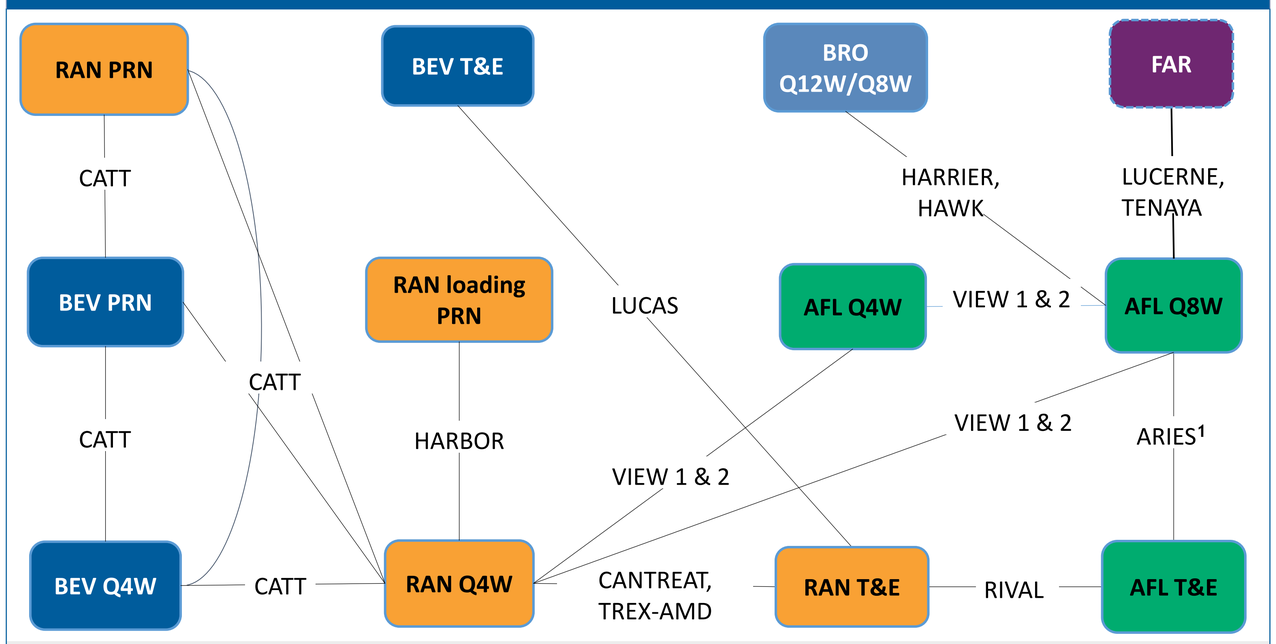


2. Baseline Characteristics



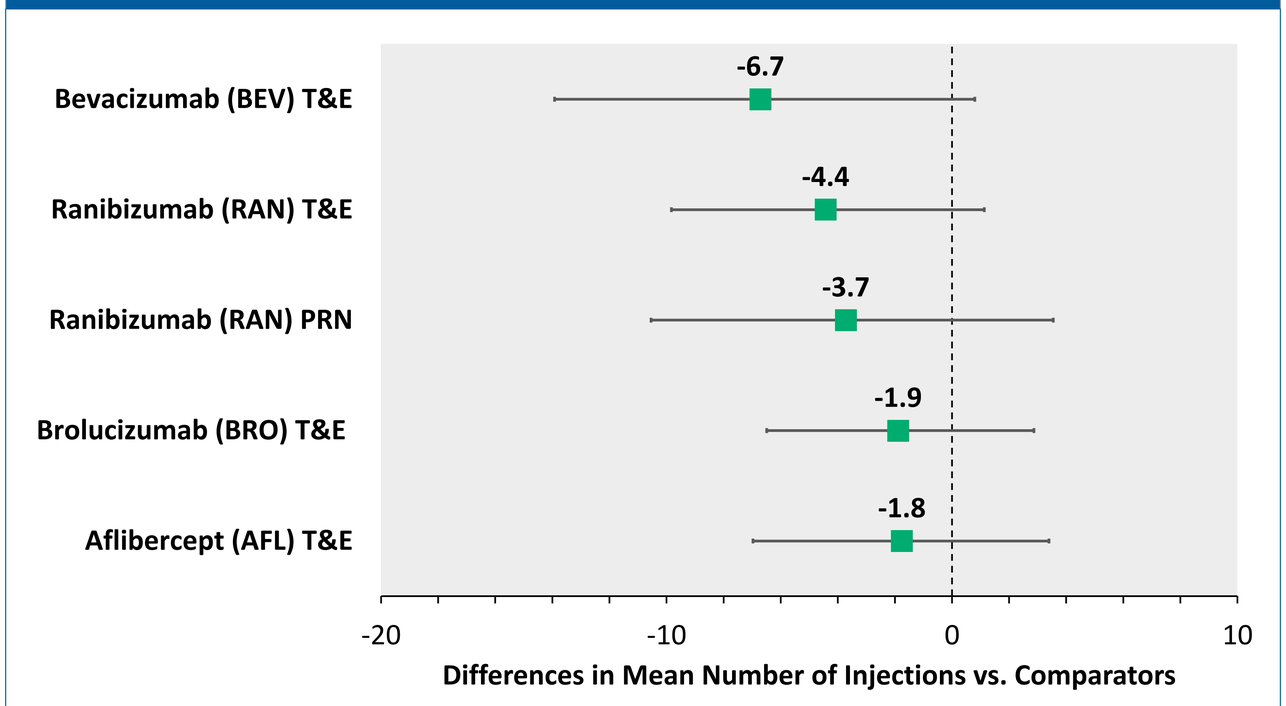
Whisker plots present the first and third quartile and the 95% Confidence interval. The ANCHOR and FOCUS trial are not included.

3. Network Diagram: Mean Number of Injections After 24 Months

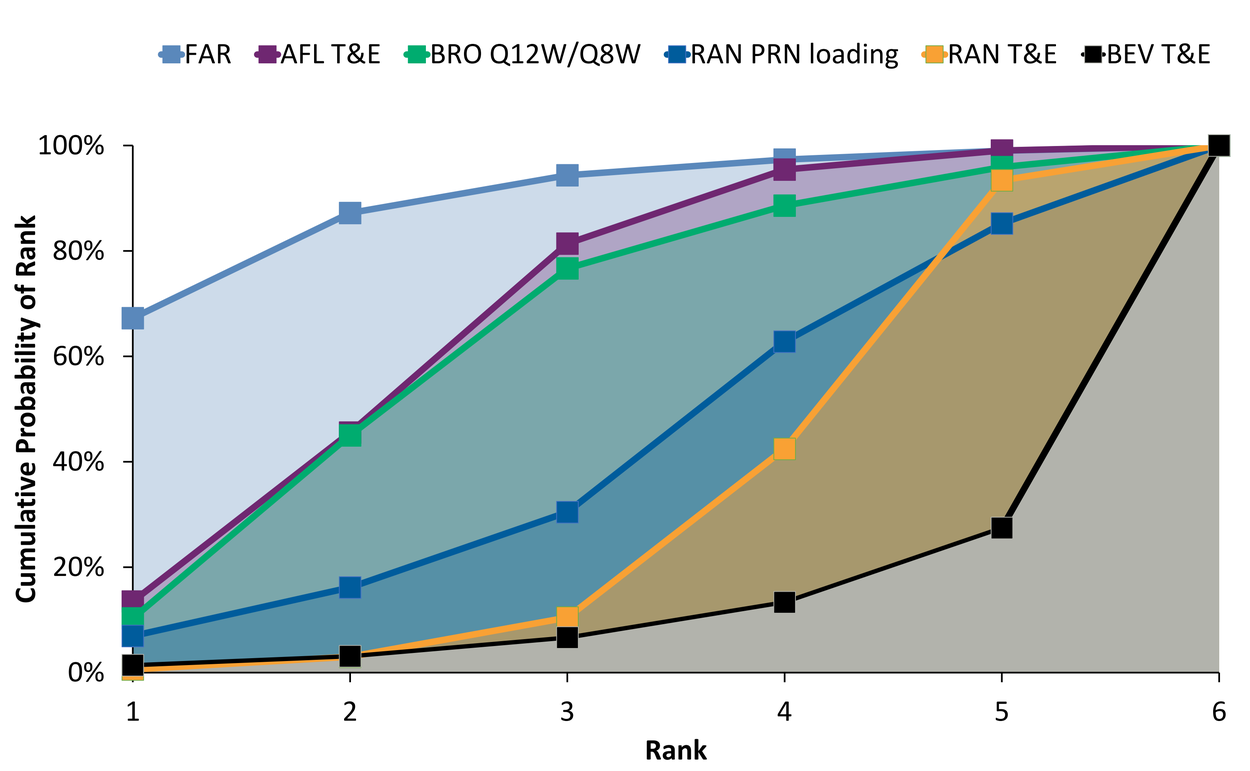


[1] In Year 2 in the ARIES trial both treatment arms switch to T&E and in VIEW 1 & 2 a switch to PRN occurs. Therefore, the 2nd year estimate for the Q8W arms was estimated using the adherence to the planned treatment schedule observed in year 1.

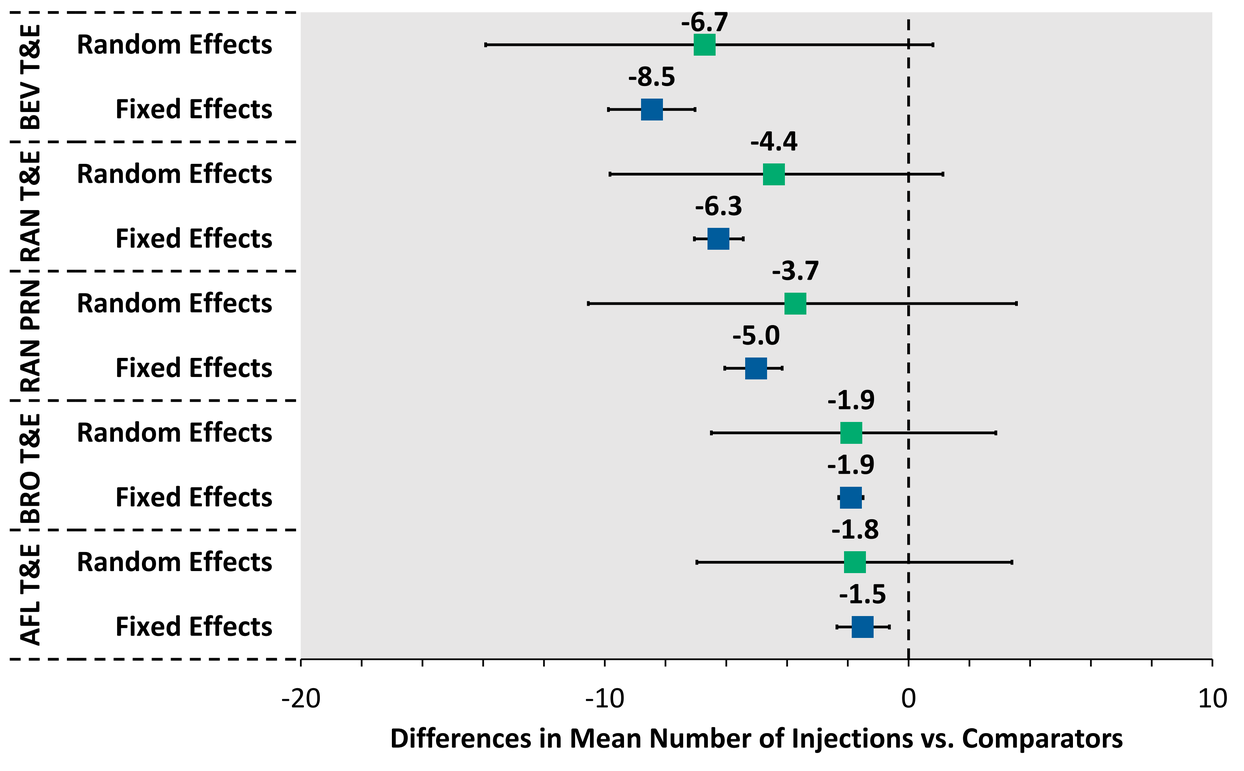
4. Forest Plot of Differences and 95% credible intervals of Faricimab vs. Other Flexible Regimens: Mean Number of Injections After 24 Months



5. SUCRA Plot



6. Sensitivity Analysis – Forest Plot for Random Effects vs. Fixed Effects Model



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Financial Disclosures

Al authors except Claire Watkins are employees of F. Hoffmann-La Roche Limited. Claire Watkins received funds for conducting the analysis.

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