The effect of four loading intravitreal aflibercept injections on macular fluid in treatment-naïve neovascular age-related macular degeneration

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Background and Purpose: Based on the VIEW studies, aflibercept therapy is initiated as a loading phase of monthly intravitreal doses for 3 months and then extended to 8-weekly dosing for treatment of nAMD. The effect of a 4th loading aflibercept injection is not known. This is relevant now because of the trial design of TENAYA and LUCERNE that evaluated the role of faricimab in exudative nAMD. Aflibercept was used as a comparator, but patients randomised to the faricimab arm received four loading injections. We aimed to evaluate the effect of four versus three loading aflibercept injections on macular fluid resolution and visual acuity (VA) in exudative nAMD.

Design: Multicentre, retrospective cohort study. from 4 centres across the UK. This service evaluation was approved by the clinical effectiveness department (CA23/MR/1234). Data collected from December 2019 to August 2021.

Participants: Inclusion criteria were consecutive patients with treatment naïve nAMD who underwent 4 loading aflibercept injections from 2 sites and with VA and OCT done at 12 and 20 weeks after first aflibercept injection. A cohort from 2 more sites that received 3 loading injections and reviewed 8 weeks post loading (i.e., at 16 weeks after 1st aflibercept injection) was included as a comparator.

Statistical Analysis: Data summarised with mean ± SD for continuous variables, and n (%) for categorical variables. Chi-square test was used to explore differences in proportions among categorical data in independent groups. P-values < 0.05 were considered statistically significant.

Figure 1 shows outcomes 8 weeks after 4 versus 3 aflibercept loading doses

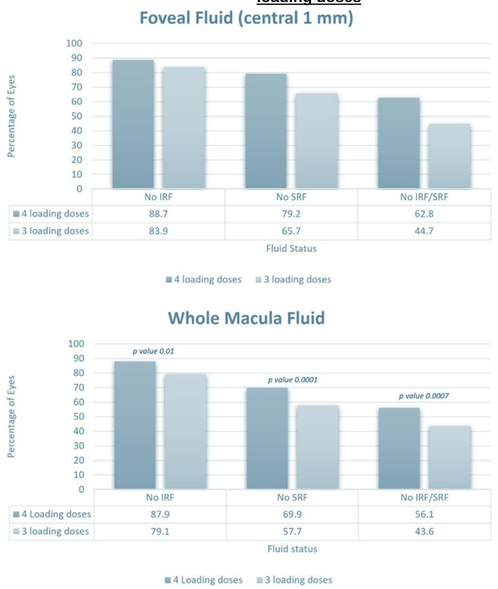


Figure 2 Comparison of fluid response to loading doses of aflibercept compared to faricimab*. Figure 2 (a), 4 weeks after 3 loading doses i.e. at 12 weeks. Figure 2 (b) 8 weeks after 4 loading doses i.e. at 20 weeks

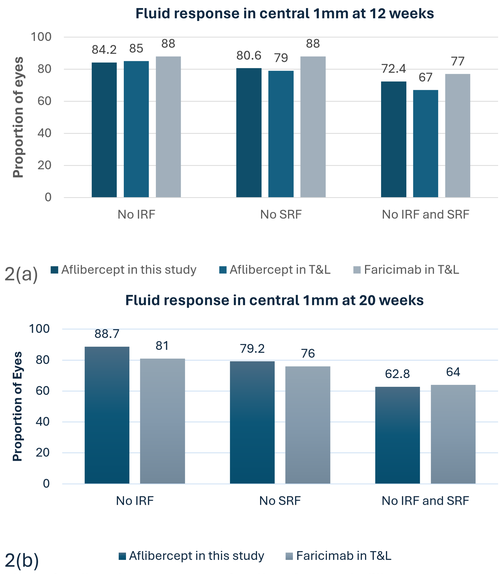


Table 1: Comparison of mean change in VA in at 8 weeks following 3 loading doses versus 4 loading doses of aflibercept

	3 loading doses of aflibercept N (%) Mean VA (SD)	4 loading doses of aflibercept N (%) Mean VA (SD)	P value
Whole cohort	640 (100%) +4.0 (11.3)	355 (100%) +5.4 (13.3)	0.09
No IRF at central 1 mm	537 (83.9%) +4.2 (11.3)	315 (88.7%) +6.1 (13.0)	0.14
No SRF at central 1 mm	421 (65.7%) +4.6 (10.9)	281 (78.6%) +5.9 (13.3)	0.08
No IRF and SRF at central 1 mm	286 (44.7%) +5.0 (11.0)	223 (62.8%) +5.8 (13.0)	0.32

Main Outcome Measure: Outcomes included the proportions of patients in 4 loading injections group with no IRF, no SRF or neither IRF or SRF (12 weeks and 20 weeks post-first aflibercept injections. The VA outcomes were also compared between the two loading regimes

Results:

- Of the 1104 patients included in the study, 995 eyes of 995 analysed. Total 355 eyes of 355 patients who received 4 loading doses of aflibercept and 640 eyes of 640 patients who received 3 loading doses of aflibercept
- The proportion of eyes with whole dry macula at 12 weeks was studied in the cohort that received 4 loading injections (N = 355). There were 85.1% eyes with no IRF and 77% with no SRF and 67% had neither IRF or SRF.
- The proportion of eyes without IRF (p value 0.04), SRF (p value 0.0001) or any IRF/SRF (p value 0.0001) were significantly higher in the eyes that received 4 loading dose injections.
- There was no statistically significant difference in change in mean VA in all the groups.

Conclusion: In summary, 4 loading dose injections of aflibercept 2mg results in a higher proportion of eyes with dry macula when compared to those receiving 3 loading dose injections when assessed at 8 weeks post last injection.

The visual outcomes were better in the cohort receiving 4 loading injections; however, this difference was not statistically significant.

*Heier JS et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomised, double-masked, phase 3, non-inferiority trials. Lancet. 2022;399(10326):729-740.

Commercial Relationships Disclosure: *Shruti Chandra reported receiving grant from Boehringer Ingelheim. SC has been on advisory board for Bayer. Sobha Sivaprasad reported receiving financial support from AbbVie, Amgen, Apellis, Bayer, Biogen, Boehringer Ingelheim, Novartis, Eyebiotech, Eyepoint Phamaceuticals, Janssen Pharmaceuticals, Nova Nordisk, Optos, Ocular Therapeutix, Kriya Therapeutics, OcuTerra, Roche, Stealth Biotherapeutics. Sanofi. Geeta Menon has conducted consultancy-advisory boards for Novartis, Bayer and Allergan, received educational travel grants from Novartis, Bayer, Allergan. Ajay Kotagiri received financial support from Bayer, Novartis and Roche.Benjamin Burton has been on advisory boards and received international conference attendance sponsored by Novartis, Roche and Bayer.*

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