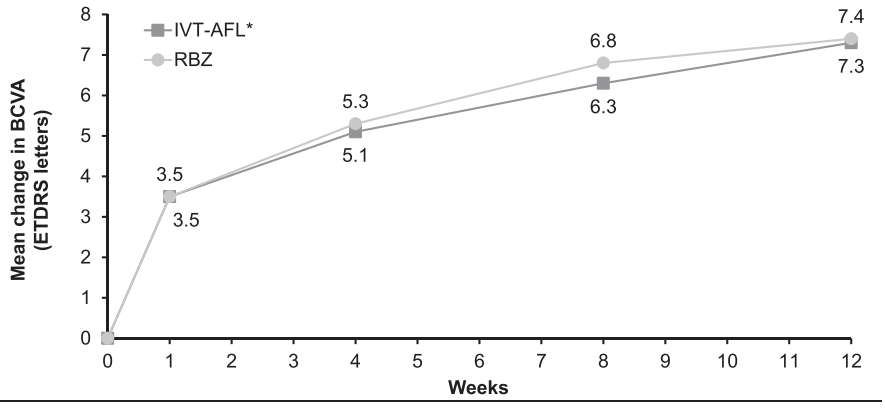
First-dose effects with intravitreal aflibercept in wet age-related macular degeneration: post-hoc analysis of VIEW-1 and VIEW-2 phase 3 studies

A post-hoc analysis of data from the VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD (VIEW) studies[1] was conducted after publication of best-corrected visual acuity (BCVA) data from the Development of Macular Atrophy in Patients with Neovascular Age-Related Macular Degeneration: A Comparison of Ranibizumab and Aflibercept (RIVAL) study. BCVA results from RIVAL suggested (although not a predefined endpoint) a delayed improvement with intravitreal aflibercept (IVT-AFL) versus ranibizumab (RBZ) in treatment-naïve patients with neovascular age-related macular degeneration (nAMD).[2] This contradicted what has been observed in other studies.[1,3–7]

RIVAL was a head-to-head study of RBZ (n=142) and IVT-AFL (n=139) using a treat-and-extend (T&E) regimen.[2] The primary endpoint was mean change in area of macular atrophy from baseline to month 24; secondary endpoints included mean change in BCVA from baseline to week (W) 52. The mean change in BCVA from baseline to W4 was numerically greater with RBZ than with IVT-AFL (2.5 vs 0.2 Early Treatment Diabetic Retinopathy Study [ETDRS] letters), a difference that persisted at W8 (5.2 vs 3.6 letters). At W52, mean change in BCVA was not statistically significant between treatment groups (7.2 vs 4.9 letters; $p = 0.06$).[2]

VIEW-1 and VIEW-2 (phase 3 randomized trials comparing the efficacy and safety of IVT-AFL and RBZ in treatment-naïve patients with nAMD) provide an opportunity to compare treatment response to IVT-AFL and RBZ in much larger studies than RIVAL, with injections matching those during treatment initiation in RIVAL.[1] Patients in the VIEW studies had active subfoveal choroidal neovascularization lesions secondary to age-related macular degeneration and baseline BCVA of 73–25 ETDRS letters.[1] Patients were randomized to IVT-AFL 0.5 mg monthly* (n = 615), 2 mg monthly (2q4; n = 617), or 2 mg every 8 weeks (2q8; n = 616) after 3 initial monthly doses, or RBZ 0.5 mg monthly (n = 609).[1] With data from VIEW-1 and VIEW-2 (pooled across studies and IVT-AFL 2q4 and 2q8 treatment groups), IVT-AFL and RBZ both provided a meaningful improvement from baseline in mean BCVA (Fig. 1), with no significant differences observed between the 2 groups at W1 and W4, or subsequently at W8 and W12 (Fig. 1).

The results of the current analysis are supported by other studies (Fig. 2) and do not support the delayed treatment effect with IVT-AFL observed in the RIVAL study. In RIVAL, although there was a large proportion of patients in the IVT-AFL arm who lost ≥10 letters in the first 4 weeks, no baseline imbalances were reported to explain this finding.[2] In the VIEW studies, BCVA improvements occurred at W1 and at each time point during the first 12 weeks in patients treated with IVT-AFL or RBZ. In a meta-analysis of observational studies, IVT-AFL and RBZ provided comparable improvements in BCVA.[7] Moreover, IVT-AFL was statistically superior among patients with a lower baseline BCVA, and a consistent improvement in BCVA was observed after 3 initial injections of IVT-AFL.[7] In an



Absolute BCVA (ETDRS letters)					
IVT-AFL	53.8	57.3	58.9	60.1	61.1
RBZ	53.9	57.3	59.2	60.6	61.3

Fig. 1—Mean change in BCVA from baseline in a pooled analysis of VIEW-1 and VIEW-2 studies in treatment-naïve patients with nAMD. *Last observation carried forward analysis:* *Combined mean BCVA values of IVT-AFL 2q4 and 2q8 treatment groups are shown. 2q4, 2 mg monthly; 2q8, 2 mg every 8 weeks; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IVT-AFL, intravitreal aflibercept; nAMD, neovascular age-related macular degeneration; RBZ, ranibizumab.

https://doi.org/10.1016/j.jcjo.2020.11.002
ISSN 0008-4182

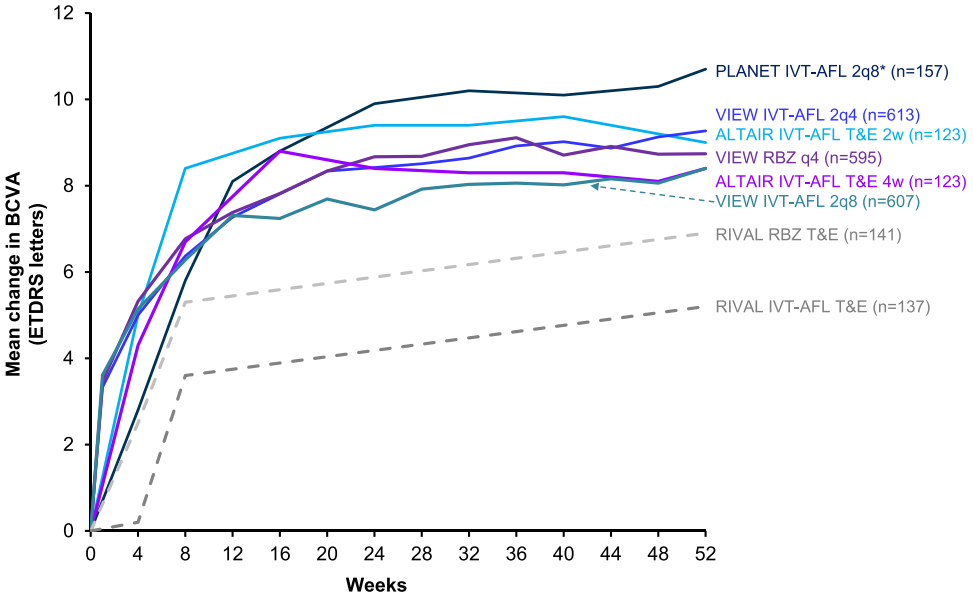


Fig. 2—Mean change in BCVA from baseline to week 52 in clinical studies of anti–vascular endothelial growth factor agents.[1–4,6] Data from multiple studies are overlaid for visual comparison only. *IVT-AFL + sham rescue photodynamic therapy group. 2q4, every 4 weeks; 2q8, every 8 weeks, after 3 initial monthly doses; 2w, 2-week adjustment group; 4w, 4-week adjustment group; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IVT-AFL, intravitreal aflibercept; q4, every 4 weeks; RBZ, ranibizumab; T&E, treat-and-extend.

indirect treatment comparison, patients treated with IVT-AFL in a T&E regimen achieved and maintained improvements in functional outcomes with fewer injections over 2 years, compared with a RBZ T&E regimen.[5] In conclusion, this post-hoc analysis and other studies underscore the similar improvements in BCVA with IVT-AFL and RBZ during the first 12 weeks of treatment in patients with nAMD.

Amin Kherani, MD, FRCSC,* Lynne R. Brunck, PhD,† Todd A. Katz, MD,‡ John Galic, MD, FRCSC§

*University of Calgary, Calgary Retina Consultants, and Southern Alberta Eye Center, Calgary, Alta.; †Bayer Consumer Care AG, Basel, Switzerland; ‡TAK Consulting LLC, New York, NY; §Royal Victoria Hospital, Montreal, Que.

Originally received Oct. 9, 2020. Accepted Nov. 3, 2020.

Correspondence to Amin Kherani, MD, University of Calgary, Calgary Retina Consultants, and Southern Alberta Eye Center, Calgary, Alta, T2H 0C8.; amin.kherani@calgaryretina.ca.

References

1. Heier JS, Brown DM, Chong V, et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 2012;119:2537–48.
2. Gillies MC, Hunyor AP, Arnold JJ, et al. Effect of ranibizumab and aflibercept on best-corrected visual acuity in treat-and-extend for neovascular age-related macular degeneration: a randomized clinical trial. JAMA Ophthalmol 2019;137:372–9.
3. DeCroos FC, Reed D, Adam MK, et al. Treat-and-extend therapy using aflibercept for neovascular age-related macular degeneration: a prospective clinical trial. Am J Ophthalmol 2017;180:142–50.
4. Lee WK, Iida T, Ogura Y, et al. Efficacy and safety of intravitreal aflibercept for polypoidal choroidal vasculopathy in the PLANET study: a randomized clinical trial. JAMA Ophthalmol 2018;136:786–93.
5. Ohji M, Lanzetta P, Korobelnik JF, et al. Efficacy and treatment burden of intravitreal aflibercept versus ranibizumab treat-and-extend regimens at 2 years: network meta-analysis incorporating individual patient data meta-regression and matching-adjusted indirect comparison. Adv Ther 2020;37:2184–98.
6. Ohji M, Takahashi K, Okada AA, et al. Efficacy and safety of intravitreal aflibercept treat-and-extend regimens in exudative age-related macular degeneration: 52- and 96-week findings from ALTAIR. Adv Ther 2020;37:1173–87.
7. Zhang Y, Chioreso C, Schweizer ML, Abramoff MD. Effects of aflibercept for neovascular age-related macular degeneration: a systematic review and meta-analysis of observational comparative studies. Invest Ophthalmol Vis Sci 2017;58:5616–27.

Footnotes and Disclosure

*IVT-AFL 0.5 mg monthly is not a commercially available dose.

A.K. is a consultant for AbbVie, Alcon, Bayer, Bausch & Lomb, and Novartis. L.R.B. is an employee of Bayer Consumer Care AG. T.A.K. is an employee of TAK Consulting and a former employee of Bayer US. J.G. declared no conflicts of interest.

Funding for the current analysis was provided by Bayer Consumer Care AG, Basel, Switzerland. The sponsor participated in the design and conduct of this analysis and preparation of the manuscript. Medical writing assistance was provided by Mia Cahill and Sarah Feeny (Apothecom), and was funded by Bayer Consumer Care AG, Basel, Switzerland.