Risk of intraocular inflammation following intravitreal injection of anti-vascular endothelial growth factor agents: a network meta-analysis

Nikhil S. Patil MD(C)[1], Arjan S. Dhoot BMSc MD(C)[2], Marko M. Popovic MD MPH(C)[3], Peter J. Kertes MD CM FRCSC[3,4], Rajeev H. Muni MD MSc FRCSC[3,5]

[1]Michael DeGroote School of Medicine, McMaster University; [2]Faculty of Medicine, University of Toronto; [3]Department of Ophthalmology and Vision Sciences, University of Toronto; [4]John and Liz Tory Eye Centre, Sunnybrook Health Sciences Centre; [5]Department of Ophthalmology, St. Michael's Hospital/Unity Health Toronto

Purpose

- The relative incidence of intraocular inflammation (IOI) between intravitreal anti-vascular endothelial growth factor (VEGF) agents for the treatment of neovascular age-related macular degeneration (nAMD) is not well established.
- Recent reports suggest an increased incidence of IOI with brolucizumab.
- A better understanding of the risk of ocular inflammatory adverse outcomes can help inform treatment paradigms in the management of nAMD, particularly in the context of recent brolucizumab findings.
- This network meta-analysis investigates the risk of IOI following intravitreal anti-VEGF injections.

Methods

- A systematic literature search was performed on Ovid MEDLINE, EMBASE, and Cochrane Library from 2005 to April 2021.
- RCTs comparing IOI incidence following intravitreal bevacizumab, ranibizumab, brolucizumab, or aflibercept for nAMD were included.
- Primary outcomes were the incidence of sight-threatening IOI (i.e. endophthalmitis, retinal vasculitis, retinal vascular occlusions) and best corrected visual acuity (BCVA).
- Secondary outcomes included the incidence of iritis/iridocyclitis, vitritis/vitreous cells, vitreous haze/floaters, and generalized intraocular inflammation.

Results

- 14 RCTs reporting on 6759 eyes at baseline were included.
- No significant differences were observed between anti-VEGFs for sight-threatening IOI.
- Compared to aflibercept, brolucizumab was associated with a significantly higher incidence of generalized IOI (RR=6.24, 95% CI=[1.40,27.90]) and vitreous haze/floaters (RR=1.64, 95% CI=[1.00,2.67]).
- There were no significant differences between comparators for other secondary outcomes.

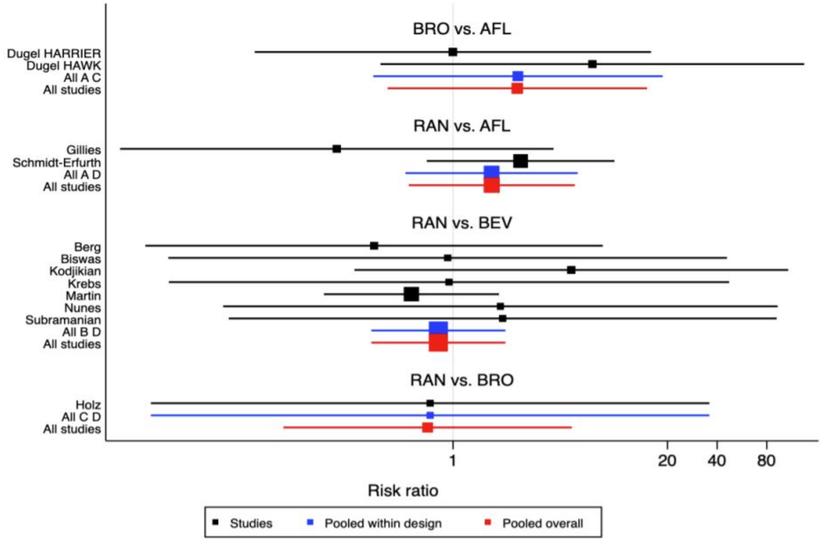

Figure 1. Endophthalmitis Forest Plot

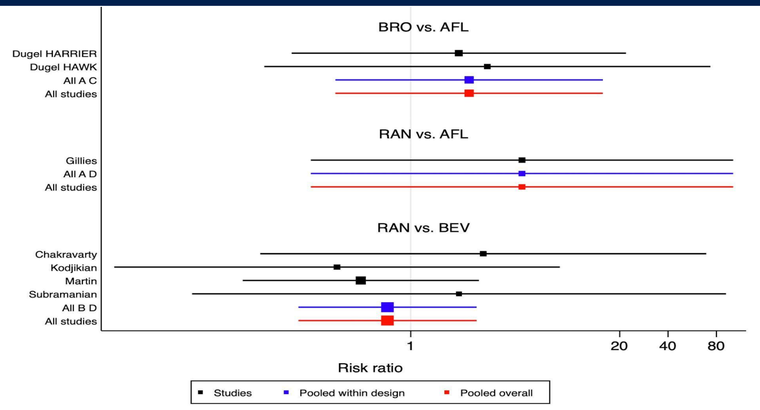

Figure 2. Retinal Vascular Occlusion Forest Plot

Discussion

- There were no significant differences between anti-VEGF agents for sight-threatening IOI and BCVA.
- There was a significantly higher risk of generalized IOI and vitreous haze/floaters following brolucizumab relative to aflibercept.
- Brolucizumab is a significantly smaller molecule than other anti-VEGF agents, which may allow for high ocular concentrations in the eye and thus a risk of IOI.
- Alongside other recent brolucizumab safety findings, our analysis suggests the need for further investigation in the use of brolucizumab for the treatment of nAMD.
- Conclusions derived at the study level may not always hold true at the individual patient level.

Conflicts of Interest

N.P: None Declared, A.D: None Declared, M.P: PSI Foundation, R.M: Bayer, Novartis, P.K: Bayer, Roche, Novartis, ArcticDx