Research Brief: Anti-vascular endothelial growth factor (anti-VEGF) drugs for the treatment of retinal conditions

Summary

We conducted a systematic review to examine the comparative effectiveness and safety of anti-VEGF drugs for the treatment of retinal conditions. Overall, 30 studies were included. Our findings suggest no statistically significant difference in terms of improvement of vision in wet AMD patients in response to ranibizumab (R), bevacizumab (B), or aflibercept (A) treatment. Similarly, in DME patients, there were no significant differences between R and B for visual acuity and vision-related outcomes. A single trial found A to have a statistically significant improvement in visual acuity outcomes compared to R and B, but this difference was deemed not clinically meaningful. Few studies evaluated the efficacy of anti-VEGF drugs in patients with RVO and CNV. Though R, A, and B seem to have a similar safety profile in the wet AMD and DME populations, this finding should be interpreted with caution given the paucity of harms data.

Implications

Our results suggest that ranibizumab and bevacizumab have similar effects on visual acuity and other vision-related outcomes in patients with wet AMD, DME, RVO, or CNV. A major limitation of this study is the lack of data for some conditions (RVO and CNV), as well as for the comparison of aflibercept with bevacizumab. This meant that certain comparisons were not possible to evaluate through meta-analysis. Though our study did not reveal any differences with respect to potential harms, none of the included studies were specifically designed to evaluate safety of anti-VEGF drugs, and there were limited data on harms.

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What is the current practice for treating retinal conditions?

- Aflibercept (A), ranibizumab (R), and bevacizumab (B) are anti-VEGF drugs currently available in Canada. However, only the first two have been approved for intravitreal use to inhibit abnormal blood vessel growth in the retina.
- We aimed to assess the effectiveness and safety of anti-VEGF drugs for retinal conditions: wet age-related macular degeneration (**wet AMD**), diabetic macular oedema (**DME**), macular oedema due to retinal vein occlusion (**RVO**) or choroidal neovascularization (**CNV**) due to pathologic myopia.

How was the study conducted?

- We compiled a protocol with input from the Canadian Agency for Drugs and Technology in Health, clinical experts, patient groups, and industry stakeholders.
- Multiple electronic databases, trial registries and grey literature were searched.
- Randomized clinical trials (RCTs) of anti-VEGF vs. each other, sham or no treatment amongst adults (age ≥ 18 years) with wet AMD, DME, RVO or CNV were eligible.
- Screening of titles, abstracts and full-text articles, data abstraction, and risk-of-bias assessment were conducted independently by 2 reviewers, and meta-analyses were conducted if ≥2 studies were available.

What did the study find?

- Thirty RCTs were included (13 wet AMD, 5 DME, 9 RVO, and 3 CNV). The results are summarized in the table below:

Population	*Outcome*	*Comparison*		
		R vs. B	**R vs. A**	**A vs. B**
Wet AMD	**Vision gain:**	No SSD (7 RCTs)	No SSD (2 RCTs)	No data
	Vision loss:	No SSD (9 RCTs)	No SSD (2 RCTs)	No data
	MD BCVA:	No SSD (8 RCTs)	No SSD (2 RCTs)	No data
	Harms:	No SSD (8 RCTs - SAE; 1 RCT - RD, IIOP, AE; 3 RCTs - VTE, WDAE; 6 RCTs - mortality; 4 RCTs - ATE; 2 RCTs - BE)	No SSD (2 RCTs - ATE, IIOP; 1 RCT - VTE, BE, RD)	No data
DME	**Vision gain:**	No SSD (1 RCT)	SSD (1 RCT)*	SSD (1 RCT)*
	Vision loss:	No SSD (1 RCT)	No SSD (1 RCT)	No SSD (1 RCT)
	MD BCVA:	No SSD (2 RCTs)	SSD (1 RCT)*	SSD (1 RCT)*
	Harms:	No SSD (1 RCT -IIOP, SAE, ATE & mortality)	No SSD (1 RCT - IIOP, ATE, SAE, & mortality)	No SSD (1 RCT - IIOP, ATE, SAE, & mortality)
RVO	**Vision gain:**	No SSD (2 RCTs)	No data	No data
	Vision loss:	No data	No data	No data
	MD BCVA:	No SSD (2 RCTs)	No data	No data
	Harms:	No SSD (1 RCT; IIOP, SAE)	No data	No data
CNV	**Vision gain:**	No SSD (1 RCT)	No data	No data
	Vision loss:	No data	No data	No data
	MD BCVA:	No SSD (2 RCTs)	No data	No data
	Harms:	No data	No data	No data

Note: R, ranibizumab; B, bevacizumab; A, aflibercept; SSD, statistically significant difference; MD BCVA, mean difference in best corrected visual acuity; IIOP, increased intraocular pressure; SAE, serious adverse events; AE, adverse events; WDAE, withdrawals due to adverse events; RD, retinal detachment; VTE, venous thromboembolic events; ATE, arterial thromboembolic events; BE, bacterial endophthalmitis.
*SSD but not clinically meaningful difference

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