INAHTA Brief

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Title Anti–Vascular Endothelial Growth Factor Drugs for the Treatment of Retinal Conditions

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Reference Anti–vascular endothelial growth factor drugs for the treatment of retinal conditions. Ottawa: CADTH; 2016 Apr. (CADTH therapeutic review; vol. 3, no. 2b)

Aim

To evaluate the comparative efficacy, safety, and cost-effectiveness of bevacizumab, ranibizumab, and aflibercept for treating patients with the following retinal conditions:

- Neovascular (wet) age-related macular degeneration (AMD)
- Diabetic macular edema (DME)
- Macular edema due to retinal vein occlusion (RVO)
- Choroidal neovascularization (CNV) secondary to pathologic myopia (PM).

Conclusions and Results

A total of 30 randomized controlled trials (RCTs) were included in the systematic review: 13 for wet AMD, five for DME, nine for RVO, and three for CNV due to PM. Most of the included studies measured efficacy using the Early Treatment Diabetic Retinopathy Study (ETDRS) scale, with a change of 15 or more ETDRS letters considered to be clinically meaningful.

Results from the systematic review, direct meta-analysis, and indirect treatment comparison suggest that bevacizumab, ranibizumab, and aflibercept have similar efficacy in patients with wAMD, DME, RVO, or CNV due to PM. One of the included studies, Wells 2015, showed greater improvement in visual acuity with the use of aflibercept over the other two drugs in patients with DME. However, that improvement was a 2.1 ETDRS-letter gain compared with ranibizumab and a 3.6 ETDRS-letter gain compared with bevacizumab, which is considerably below the threshold of clinically meaningful change.

Regarding safety (e.g. serious adverse events, endophthalmitis, arterial thromboembolism, etc.), the systematic review and meta-analysis showed no statistically significant differences among the included anti–vascular endothelial growth factor (anti-VEGF) drugs. To complement the evidence derived from RCTs, this review also included supplemental information from a structured review of real-world evidence. It suggests that there is no statistical significantly increased incidence of ophthalmic or cardiac adverse events as long as bevacizumab aliquots are prepared and handled appropriately.

The pharmacoeconomic analysis compared the relative cost of each product, as clinical evidence suggested no differences in the efficacy and safety of the included anti-VEGF drugs. Costs of therapy depend on the condition being treated and the duration of therapy, but in general, total treatment costs per patient are $6,092 to $20,887 for aflibercept; $580 to $3,397 for bevacizumab; and $6,720 to $39,360 for ranibizumab.

Recommendations

Available in a separate report, from:
https://www.cadth.ca/sites/default/files/pdf/TR0009_Anti-VEGFs_Recs_Report.pdf

Methods

Peer-reviewed literature searches were used to identify potential RCTs evaluating bevacizumab, ranibizumab, and aflibercept in patients with wAMD, DME, RVO, or CNV due to PM. Paired reviewers conducted literature screening, assessment of quality, and data extraction independently; any disagreement was resolved through adjudication. Direct meta-analysis and Bayesian indirect comparison were conducted for applicable efficacy and safety outcomes. A series of cost-minimization analyses was conducted for each indication, with areas identified as uncertain explored in selectivity analyses.

Further Research or Reviews Required

Considering that the included RCTs were not designed with sufficient power to detect harms, large randomized trials with several years of follow-up would provide a clear answer regarding the relative safety of the anti-VEGF drugs. Such trials would benefit from a multi-arm randomized trial design that examines the three anti-VEGF agents simultaneously. Finally, a gap in the available evidence relates to the safety of procedures used to prepare, distribute, and store bevacizumab aliquots.

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