TITLE: Bevacizumab or Ranibizumab for Treatment of Diabetic Retinopathy: Clinical Effectiveness

DATE: 21 January 2010

RESEARCH QUESTION:

What is the clinical effectiveness of bevacizumab or ranibizumab for treatment of diabetic retinopathy?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 4, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2005 and January 2010. No filters were applied to limit the retrieval by study type. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCT), controlled clinical trials, and observational studies.

One systematic review, 11 RCTs, and one controlled clinical trial were identified regarding the clinical effectiveness of bevacizumab for treatment of diabetic retinopathy. No relevant articles were identified regarding the clinical effectiveness of ranibizumab for the treatment of diabetic retinopathy. Due to the availability of studies associated with higher internal validity,
observed studies were moved to the appendix. Additional articles of potential interest may also be found in the appendix.

OVERALL SUMMARY OF FINDINGS:

Bevacizumab and ranibizumab are anti-vascular endothelial growth factor (VEGF) agents not currently approved for the treatment of diabetic retinopathy (DR) and its complications. A systematic review regarding the use of anti-VEGF therapy for treatment of diabetic macular edema (DME) found these drugs to be favored when compared to sham treatments; however, the differences were not statistically significant and there was not enough available evidence for authors to recommend the use of anti-VEGF therapy for DME.

Two RCTs and one controlled clinical trial regarding the use of preoperative intravitreal bevacizumab (IVB) injection were identified. Patients with proliferative DR were injected with IVB preoperatively for the prevention of postvitrectomy hemorrhage. Treatment groups showed lower rates of hemorrhage at one week and one month when compared to the controls. Intravitreal bevacizumab decreased the incidence of early postvitrectomy hemorrhage in diabetic patients. Treatment with IVB reduced regression of neovascularization after one week. Improved visual acuity was observed at last follow-up visit in patients who received 2.5 mg IVB three to five days before vitrectomy.

Administration of IVB at the time of cataract surgery (phacoemulsification plus intraocular lens implantation) resulted in DR progression in 45.45% of eyes in the control group and 11.42% of eyes in the treatment group. The authors concluded that IVB administered at the time of surgery is safe and effective for the prevention of DR progression. When IVB was administered immediately after phacoemulsification for DME, the recorded best-corrected visual acuity (BCVA) was better in the treatment group and there was a significant difference in mean macular thickness between the two groups at both three and six months follow-up. The authors concluded that IVB prevents worsening of DME in diabetic patients undergoing cataract surgery and demonstrates effectiveness in the short-term.

When comparing macular laser photocoagulation versus IVB versus IVB plus triamcinolone acetonide (IVT), a significant improvement in treatment outcome was observed in the IVB group at all follow-up visits and in the IVB/IVT combination treatment group at both six and 12 week follow-up. A significant decrease in central macular thickness was observed in all groups up to six weeks. Patients receiving IVB and IVB/IVT showed better visual outcomes than patients who underwent photocoagulation alone. The observed treatment response for IVB was short-term.

Laser treatment with or without the addition of IVB was also investigated. Of the eyes in the treatment group (IVB + laser therapy), 87.5% showed complete regression of DR at six weeks follow-up versus 25% of eyes in the control group (laser); however, the proportion of patients showing regression in the two groups were identical by week 16. In patients who had not undergone any prior laser treatments, the addition of IVB to photocoagulation resulted in a significant decrease in the area of actively leaking new vessels. The addition of IVB to photocoagulation treatment showed no short-term benefit.
When two doses of IVB were compared (1.25 mg versus 2.5 mg) for treatment of DME, a significant decrease in mean BCVA was observed in both treatment groups at six months. There was also significant improvement in both central foveal thickness and BCVA. IVB was more effective in eyes that had not been previously treated for DME and both doses of IVB showed similar results. When treatment with IVT was compared IVB for DME, central macular thickness and visual acuity were improved in the IVT group. The authors of this study suggested a single dose of IVT may be more effective for short-term management of DME than IVB.

Overall, treatment with IVB was associated with decreased incidence of early postvitrectomy hemorrhage in diabetic patients, increased visual acuity, decreased mean macular thickness, and resulted in a significant decrease in the area of actively leaking new vessels.
REFERENCES SUMMARIZED:

Health technology assessments
No literature identified

Systematic reviews and meta-analyses


Randomized controlled trials


Bevacizumab or Ranibizumab for Treatment of Diabetic Retinopathy


**Controlled clinical trials**

APPENDIX – FURTHER INFORMATION:

Ongoing clinical studies


Observational studies – prospective


Bevacizumab or Ranibizumab for Treatment of Diabetic Retinopathy


Observational studies – retrospective


Coverage policies


Safety information

55. Hoffmann-La Roche Ltd. *Health Canada endorsed important safety info on Avastin (bevacizumab).* [Internet]. Ottawa: Health Canada; 2008. [cited 2010 Jan 13]. Available from:
Review articles


