Pharmacologic management of neovascular age-related macular degeneration: systematic review of economic evidence and primary economic evaluation

William Hodge,* MD, PhD, FRCSC; Allan Brown,† BSc, MBA, MA; Steve Kymes,‡ PhD, MHA; Alan Cruess,§ MD, FRCSC; Gord Blackhouse,¶ MBA, MSc; Robert Hopkins,¶ MA, MBA; Lynda McGahan,† MSc; Sanjay Sharma,** MD, MBA, MSc, FRCSC; Irene Pan,* MSc; Jason Blair,†† MD; David Vollman,‡ MD, MBA; Andra Morrison,† BSc

ABSTRACT • RÉSUMÉ

Objective: To examine the economic implications for the Canadian health system of pharmacologic treatment of neovascular age-related macular degeneration (AMD).

Design: Systematic review of economic literature and a primary economic evaluation.

Participants: Economic literature search identified 392 potentially relevant articles, 12 of which were included for final review.

Methods: Studies were included if they met the following criteria: (*i*) provision of a summary measure of the trade-off between costs and consequences; (*ii*) participants of 40 years and older with neovascular AMD; (*iii*) interventions and comparators: comparison of photodynamic therapy using verteporfin (V-PDT), pegaptanib, bevacizumab, ranibizumab, anecortave acetate, intravitreal triamcinolone, placebo, or clinically relevant combinations; and (*iv*) outcome reported as an incremental measure of the implication of moving from the comparator to the intervention. The following databases were searched through the OVID interface: MEDLINE, EMBASE, BIOSIS Previews, CINAHL, PubMed, Health Economic Evaluations Database (HEED), and the Cochrane Library. For the economic evaluation, we took a decision analytic approach and modeled a cost-utility analysis, conducting it as a microsimulation of a Markov model.

Results: In general, V-PDT is more cost effective than conventional macular laser, and pegaptanib is likely more cost effective than V-PDT. The primary economic analysis revealed ranibizumab to be effective but at an unacceptably high cost per quality-adjusted life year (QALY) (>$50 000 per QALY).

Conclusion: Although ranibizumab is effective for wet AMD, its cost is unacceptably high based on cost-utility theory.

Objet : Examen des implications économiques du mode de traitement pharmacologique de la dégénérescence maculaire néovasculaire liée à l'âge (DMLA), dans le système de santé canadien.

Nature : Un examen systématique de la littérature économique et une évaluation économique primaire.

Participants : La recherche dans la littérature économique a permis d'identifier 392 articles potentiellement pertinents; 12 ont été inclus dans la revue définitive.

Méthodes : Ces études devaient respecter les critères que voici : (*i*) provision d'une mesure sommaire de compromis entre les coûts et les conséquences; (*ii*) participants de 40 ans et plus avec DMLA néovasculaire; (*iii*) interventions et comparables : comparaison de la thérapie photodynamique à l'aide de verteporfin (V-PDT), pégaptanib, bévacizumab, ranibizumab, acétate d'anecortave, triamcinolone intravitréen, placébo ou combinaisons cliniquement pertinentes; et (*iv*) résultats signalés comme mesures incrémentielles de l'implication du changement du comparable à l'intervention. Les bases de données qui suivent ont fait l'objet de la recherche par l'interface *OVID : MEDLINE, EMBASE, BIOSIS Previews, CINAHL, PubMed, Health Economic Evaluations Database (HEED)* et *Cochrane Library*. Aux fins de l'évaluation économique, nous avons pris une approche analytique décisionnelle et avons modélisé une analyse coût-utilité, sous forme de microsimulation d'un modèle de Markov.

Résultats : En règle générale, le V-PDT est plus rentable que le laser maculaire conventionnel, et le pégaptanib est vraisemblablement plus rentable que le V-PDT. L'analyse économique primaire a révélé que le ranibizumab est plus efficace mais à un coût élevé inacceptable par année de vie qualité ajustée (QALY) (>50 000 $ par QALY).

Conclusion : Bien que le ranibizumab soit efficace pour la DMLA humide, son coût élevé est théoriquement inacceptable sur une base de coût-efficacité.

From *the Department of Ophthalmology, University of Western Ontario, London, Ont.; †the Canadian Agency for Drugs and Technologies in Health, Ottawa, Ont.; ‡the Department of Ophthalmology and Visual Sciences, Washington University School of Medicine, St. Louis, Mo.; §the Department of Ophthalmology and Visual Sciences, Dalhousie University, Halifax, N.S.; ¶the Programs for Assessment of Technology in Health (PATH) Research Institute, McMaster University, Hamilton, Ont.; **the Departments of Ophthalmology and Epidemiology, Queen's University, Kingston, Ont.; and ††the Department of Ophthalmology, University of Ottawa, Ottawa, Ont.

Correspondence to William Hodge, MD, Ivey Eye Institute, St. Joseph's Hospital, 268 Grosvenor St., London, ON N6A 4V2; William.Hodge@sjhc.london.on.ca

This article has been peer-reviewed. Cet article a été évalué par les pairs.

Can J Ophthalmol 2010;45:223–30
doi:10.3129/i10-047

Originally received Oct. 7, 2009. Final revision Mar. 15, 2010
Accepted Mar. 18, 2010
Published online May 11, 2010

Age-related macular degeneration (AMD) is the leading cause of visual loss in people older than 50 years in North America. AMD is also the leading cause of registered visual impairment in Canada. Over the next 25 years, the increase in the number of legally blind individuals aged 40 years and older is expected to be greatest for AMD (111%) but will also be substantial for open-angle glaucoma (105%) and diabetes (85%).[1] Neovascular AMD may also be subdivided angiographically into classic, predominantly classic (PC), minimally classic, and pure occult lesions.

Photodynamic therapy (PDT) using verteporfin (V-PDT) (Visudyne, Novartis Ophthalmics, Menlo Park, Calif.) has been a mainstay of therapy for neovascular AMD throughout most of this decade, especially in eyes with classic subfoveal choroidal neovascularization. Verteporfin has been approved in Canada for the treatment of AMD since 2000.[2] However, occult subtypes of choroidal neovascularization often convert to classic if left untreated. Pegaptanib (Macugen, Pfizer, Franklin Lakes, N.J.) has been approved in Canada for AMD since 2005.[3] Pegaptanib is an anti-vascular endothelial growth factor (VEGF) aptamer that binds VEGF 165, the main pathologic isoform. Newer anti-VEGF therapies are emerging, specifically ranibizumab (Lucentis, Genentech, San Francisco, Calif. and Novartis Ophthalmics, Basel, Switzerland), which has now been approved in Canada, and bevacizumab (Avastin, Genentech, San Francisco, Calif. and Roche, Basel, Switzerland), as well as a new steroid analog, anecortave acetate (Retaane, Alcon, Fort Worth, Tex.), given as a juxtascleral depot injection.

The purpose of this study was to examine the economic implications for the Canadian health system of pharmacologic treatment of neovascular AMD. A systematic review of the economic literature was undertaken.

Methods

Search strategy

The following bibliographic databases were searched through the OVID interface: MEDLINE (1950 to present; In-Process & Other Non-Indexed Citations), EMBASE (1980 to present), BIOSIS Previews (1985–1989 and 1989 to present), CINAHL (1982 to present), PubMed, the Health Economic Evaluations Database (HEED), and the Cochrane Library. Controlled vocabulary and keywords used in the search included terms for AMD and the drugs of interest in this project (verteporfin, bevacizumab, pegaptanib, ranibizumab, and anecortave acetate) and their brand names. An economic filter was used to limit retrieval to relevant economic records. A detailed search strategy is available upon request.

OVID AutoAlerts were set up to send monthly updates with any new economic literature. Monthly updates were also performed in PubMed, HEED, and the Cochrane Library database. We obtained supplementary cost information for the economic model by contacting experts and researching administrative databases.

An economic evaluation was included for review if it satisfied all of the following criteria: (*i*) provision of a summary measure of the trade-off between costs and consequences; (*ii*) adults aged 40 years or older with neovascular AMD; (*iii*) interventions and comparators: comparison of V-PDT, pegaptanib, bevacizumab, ranibizumab, anecortave acetate, intravitreal triamcinolone, placebo, or clinically relevant combinations; and (*iv*) outcome reported as an incremental measure of the implication of moving from the comparator to the intervention (e.g., a summary measure such as the incremental cost-effectiveness ratio [ICER]).

Two reviewers applied the selection criteria to the title and abstract (if available) of studies obtained in the first phase of the literature search to identify its relevance to our objective and then in the second phase for full-text articles.

One reviewer used a data-extraction sheet to extract the principal content of each included study. Data extracted from included economic studies were checked by a second reviewer.

Two reviewers used a checklist developed for the *British Medical Journal* to assess the quality of the included economic evaluations.[4] The quality measures were not formally used to quantitate results but are presented to guide reader interpretation of the available evidence.

The economic literature search identified 392 potentially relevant articles. After applying the inclusion criteria, 12 articles were included for review. Most of the articles compared V-PDT with placebo or best supportive care;[5–12] one compared bevacizumab and ranibizumab in a threshold analysis;[13] one compared anecortave acetate and V-PDT, also in a threshold analysis;[14] two compared pegaptanib with best supportive care or usual care;[12,15] and one compared pegaptanib with V-PDT and standard care.[16]

Figure 1 summarizes the QUORUM diagram for this study. Table 1 summarizes the characteristics of the included economic studies and Table 2 summarizes their results.

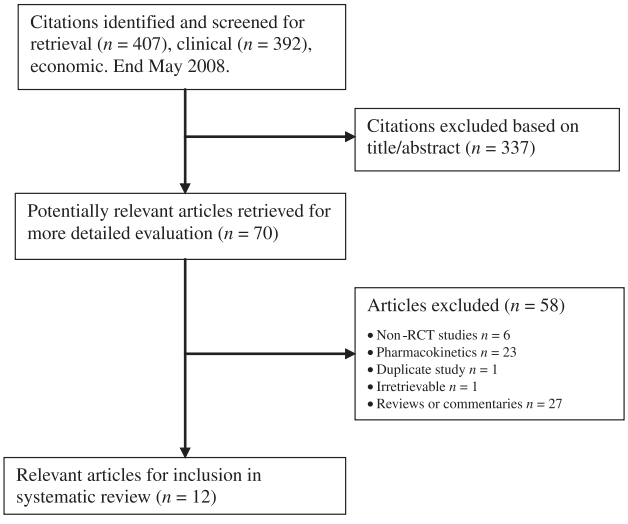

Fig. 1—QUORUM diagram. RCT, randomized control trials.