Cost-Effectiveness of Macugen Compared to Photodynamic Therapy (PDT) with Verteporfin and to Standard Care in the Treatment of Subfoveal Wet Age-Related Macular Degeneration (AMD) in the Elderly in Canada

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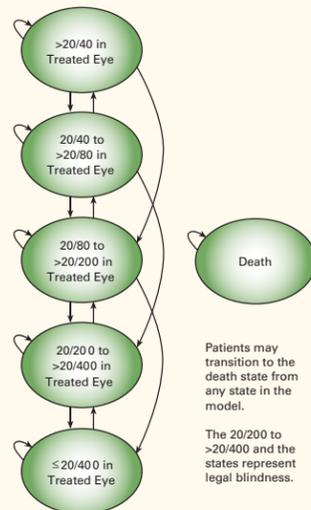
INTRODUCTION

- It is estimated that between 17,000 and 24,000 new patients are diagnosed in Canada with age-related macular degeneration (AMD) each year.[1]
- Wet AMD is the leading cause of blindness among the elderly, accounting for approximately 50% of new cases of blindness in Canada.[2]
- The resulting visual impairment affects patient quality of life as much as arthritis, asthma, diabetes, and stroke[3] and also affects the individual's emotional and social health, as well as independence.[4]
- The economic burden of AMD is high because patients with impaired vision due to AMD have an increased risk of fall,[5,6] fracture,[7] and depression[8] and need daily support services or nursing home care.
- Macugen is a new treatment for subfoveal neovascular AMD that is efficacious for all lesion subtypes (predominantly classic, minimally classic, and occult).
- Understanding the cost-effectiveness of Macugen compared to photodynamic therapy with verteporfin (PDT) and standard care[a] could assist authorities in Canada in making informed decisions about reimbursement.

OBJECTIVE

To assess the cost-effectiveness of Macugen versus PDT and of Macugen versus standard care in treating AMD.

Figure 1. Structure of Markov Model

>20/40 in Treated Eye → 20/40 to >20/80 in Treated Eye → 20/80 to >20/200 in Treated Eye → 20/200 to >20/400 in Treated Eye → ≤20/400 in Treated Eye → Death

Patients may transition to the death state from any state in the model.

The 20/200 to >20/400 and the states represent legal blindness.

METHODS

The model structure is a Markov framework in which patients transition between health states based on visual acuity in the better-seeing eye (Figure 1). Details on model scope are presented in Table 1.

- Patient age and gender distribution were obtained from Statistics Canada (2003).[9]
- Initial distribution of patients in visual acuity ranges was obtained from the VISION clinical trials.[10]
- Utility values were taken from published literature.[11]
- Therapy discontinuation was assumed to occur after 2 years or when visual acuity drops below 20/200 (treatment not considered beneficial).
- Age- and gender-specific mortality rates were estimated from Statistics Canada (2003). Relative risk of death due to blindness is 1.37,[12] and mortality was allowed to increase with patients' age.
- The number of treatments with Macugen in year 1 and year 2 was obtained from the VISION trials.[10] Average annual number of PDT treatments is extracted from the TAP Report 2.[11]
- Costs of Macugen and PDT were estimated from annual use as reported in the clinical trials[10,14-16] and physician payment schedule from the Province of Quebec[17] (Table 2).
- The fee related to an outpatient visit was derived from the Quebec health technology assessment agency.[18]
- Costs of treating adverse events (AEs) were estimated from the rates of AE occurrence taken from the clinical trials[10,14-16] and treatment patterns of AEs as estimated from interviews with clinical experts (Table 2).
- Costs of comorbidities (i.e., depression/anxiety, government-sponsored assisted living facility, and fractures) were estimated from the published literature (Table 3).

Table 1. Model Scope

Parameter	Assumption
Model time horizon	Variable. Base case is lifetime
Cycle time	3 months
Patient population	• Age groups: 65–74 and 74+ • Males and females • Lesion subtypes: predominantly classic, minimally classic, and occult
Perspective	Canadian societal
Comparators	Macugen, PDT, and standard care
Implementation	• Easy to use, easily customized model built in Microsoft Excel • Transparent with information available about sources, assumptions, and calculations

PDT = Photodynamic therapy with verteporfin

- Vision rehabilitation was defined as twelve half-day workshops provided by the Canadian National Institute for the Blind ($150 per half day). Based on clinical opinion, vision rehabilitation was assumed to occur only once in a patient's lifetime, and the percentage of patients using the services was 0%, 16%, and 48% for patients in health states >20/40 and 20/40 to >20/80, 20/80 to >20/200, and 20/200 to >20/400 and ≤20/400, respectively.
- The treatment comparators in the model are Macugen, standard care, and PDT.
- Since no head-to-head comparisons of Macugen vs. PDT exist, the incremental cost effectiveness ratio is calculated as

$$((C_{MAC} - C_{SHAM}) - (C_{PDT} - C_{PLAC})) / ((E_{MAC} - E_{SHAM}) - (E_{PDT} - E_{PLAC}))$$

where C_{MAC} and E_{MAC} are the per-patient cost and efficacy experienced by patients on Macugen within the Macugen clinical trial, C_{SHAM} and E_{SHAM} are the per-patient cost and efficacy experienced by patients on sham within the Macugen clinical trial, C_{PDT} and E_{PDT} are the per-patient cost and efficacy experienced by patients on PDT within the PDT clinical trial, and C_{PLAC} and E_{PLAC} are the per-patient cost and efficacy experienced by patients on placebo within the PDT clinical trial.

- Costs are reported in 2004 Canadian dollars (CAN$).
- Costs and outcomes are discounted at 3% per annum.

Transition Probabilities

- Three-month transition probabilities for the first and second year are estimated from the year 1 and year 2 clinical efficacy results of the VISION, VIP, and TAP trials, respectively.[14-16]
- Transitions between visual acuity levels are based on ≥3-line gain, 3- to 6-line loss, and >6-line loss on the visual acuity scale.
- After discontinuation, transition probabilities are based on sham/placebo results for the respective treatments.

Table 2. Cost of Resource Use

Parameter	Parameter Value (CAN$)
Macugen	
Year 1 costs	$10,987
Year 2 costs	$9,025
PDT	
Year 1 costs	$8,818
Year 2 costs	$6,358
Costs of treating AEs	
Endophthalmitis	$343
Injection site AE	$33
Retinal capillary nonperfusion	$462
Retinal detachment	$818
Traumatic injury to lens	$1,801
Vitreous hemorrhage	$33
Visual disturbance	$2,072

PDT = Photodynamic therapy with verteporfin, AEs = adverse events
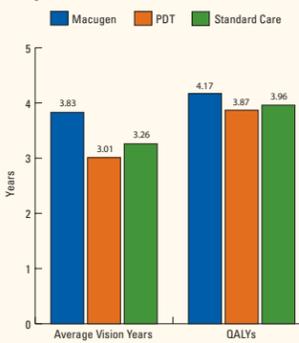
Table 3. Cost of Comorbidities

Cost of Comorbidities	Depression/Anxiety	Assisted Living	Fractures
Probability of patients with normal vision needing service*	11.10%	2.10%	3.10%
Hazard ratio of resource use by vision health state*			
>20/40	1.0	1.0	1.0
20/40 to >20/80	1.20	2.67	1.44
20/80 to >20/200, 20/200 to >20/400, ≤20/400	1.29	2.34	1.16
Annual cost of comorbidity**	$1,060	$15,701	$139

*Source: Regie de l'assurance maladie du Québec (RAMQ) database
**Sources: Comorbidity costs were obtained from Center for Addition and Mental Health (CAMH), Canadian Psychiatric Association and the Canadian Psychological Association, Community Care Access, and Ministry of Health and Long Term Care (MOHLTC) - Ontario Databases

RESULTS

Results are summarized in Figures 2 and 3 and Table 4.

Figure 2. Lifetime Patient Outcomes

Legend: Macugen | PDT | Standard Care

Average Vision Years: Macugen 3.83, PDT 3.01, Standard Care 3.26
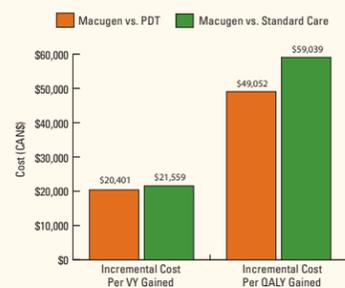QALYs: Macugen 4.17, PDT 3.87, Standard Care 3.96

Note: Outcomes are not normalized between clinical trials.

- Patients on Macugen experience more vision years[b] and quality-adjusted life years (QALYs) than patients on PDT or standard care.

Table 4. Lifetime Per-Patient Cost Outcomes (CAN$)

Cost	Macugen	PDT	Standard Care
Drug costs	$9,932	$5,569	$568
Costs associated with drug administration	$3,208	$2,996	$292
AE costs	$24	$8	$1
Costs of comorbidities	$6,852	$6,772	$6,808
Average total costs	**$20,016**	**$15,345**	**$6,737**

Note: Outcomes are not normalized between clinical trials.

- The incremental cost between treatment options is mainly driven by the cost of the drug and its administration.

Figure 3. Incremental Costs per Vision Year (VY) and QALY

Legend: Macugen vs. PDT | Macugen vs. Standard Care

Incremental Cost Per VY Gained: Macugen vs. PDT $20,401, Macugen vs. Standard Care $21,559
Incremental Cost Per QALY Gained: Macugen vs. PDT $49,052, Macugen vs. Standard Care $59,039

- Macugen is cost-effective compare to treatment with PDT or standard care.
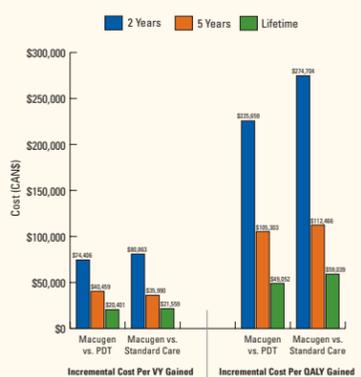
SENSITIVITY ANALYSES

- One-way sensitivity analyses were performed to test the robustness of the results when key parameters and assumptions were varied:
  - time horizon
  - cost associated with vision loss comorbidities
  - effect of vision loss on mortality
  - AMD treatment costs (excluding drug cost)
  - effect of relative prevalence of angiographic subtypes of subfoveal wet AMD
  - effect of continuing treatment after reaching legal blindness
  - age of AMD patients
  - discount rate
  - probability of resource utilization
  - utility scores

  The robustness of the base-case model was confirmed via sensitivity analyses on key parameters and assumptions.

- Variations in the model's time horizon have the greatest impact on the cost-effectiveness ratios (Figure 4).

Figure 4. Effect of Variation in Model Time Horizon on the Cost-Effectiveness Ratios

Legend: 2 Years | 5 Years | Lifetime

Incremental Cost Per VY Gained:
Macugen vs. PDT: $74,406, $40,459, $20,401
Macugen vs. Standard Care: $90,563, $35,980, $21,559

Incremental Cost Per QALY Gained:
Macugen vs. PDT: $225,809, $105,303, $49,052
Macugen vs. Standard Care: $274,159, $113,466, $59,039

- Lifetime horizon, used in the base case scenario, is the appropriate time window to consider because the impact of treatment on preserving visual acuity is expected to extend to the longer term.

CONCLUSIONS

- Macugen improves patient outcomes (vision years and QALYs) over PDT and standard care.
- Macugen is a cost-effective treatment for treating elderly patients with subfoveal wet AMD regardless of lesion subtype when compared to standard care and PDT with verteporfin.

FUNDING

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a Standard care is defined as treatment with either PDT that was allowed at the discretion of the treating clinician or no treatment, as seen in actual practice and in the sham arm of the Macugen clinical trial.

b Vision years are defined as the number of years a patient has a visual acuity greater than the definition of legal blindness, 20/200.