An Economic Evaluation of Ranibizumab for the Treatment of Neovascular (wet) AMD in the United Kingdom

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Introduction

Neovascular (wet) age-related macular degeneration (nAMD), is a degenerative disease affecting mostly older adults and is a leading cause of blindness in the developed world. In the United Kingdom (UK) the prevalence of Wet AMD is 284,000 with 39,700 new cases a year[1].

Both ranibizumab and aflibercept have demonstrated efficacy in the treatment of nAMD. The aim of this analysis was to evaluate the cost-effectiveness of ranibizumab compared with aflibercept for the treatment of nAMD from the UK healthcare provider perspective.

Methods

Within this analysis a patient-level simulation model was developed. Many aspects of an eye disease model lend itself to a patient-level simulation (PS) approach, most notably the ability to model two eyes – the interplay between the visual acuity in each eye and quality of life, and incorporating bilateral disease. Despite the potential advantages of a PS approach all recent nAMD HTA submissions to NICE have used a Markov approach, but have effectively been one-eye models, attracting criticism from NICE. Outcomes were modelled on a remaining-lifetime time horizon. Future costs and health outcomes were discounted at 3.5% per annum.

Patients were assumed to receive either ranibizumab or aflibercept over a maximum of 5 years. The model was based on the licensed posologies for each drug.

The model was driven by best corrected visual acuity score (BCVA). Baseline patient characteristics were based on the EXCITE Phase III study[2] due to the availability of data in both eyes. In Year 1 and Year 2, response to ranibizumab treatment was based on data from the IVAN study[3], a large, independent randomized trial conducted in the UK. The relative effectiveness of aflibercept was based on a network meta-analysis. Within the NMA, response to treatment (defined by mean change from baseline in BCVA) was modelled on a monthly basis up to 24 months.

Beyond 24 months, BCVA was assumed to remain constant up to 60 months as per the assumption employed in NICE TA294. After this period, or after treatment discontinuation, vision in the study eye was assumed to decline gradually, derived from Wong et al. (2008)[4]. Natural history data for the general population was used to model the untreated eye. BCVA change in each eye was modelled independently. A probability of developing bilateral disease was applied throughout the model. It was assumed patients could discontinue treatment at any time in the five year period. Probabilities of discontinuation were based on the rate of withdrawal not due to death.[7]

To estimate quality of life, a real world dataset was obtained from Czoski-Murray (2009)[5], a study that used contact lenses to simulate the effect of visual impairment. A regression analysis was undertaken to estimate the utility as a function of the visual acuity in both eyes and assuming correlation between eyes.

The key costs considered in the analysis included drug costs, costs of administering the drugs and monitoring costs. Costs were also applied as patients entered the blindness health state (below 35 letters). To reflect the increased mortality risk in patients who have some degree of impaired vision, a relative risk was applied to the background mortality rate, based on data from Christ (2008)[6].

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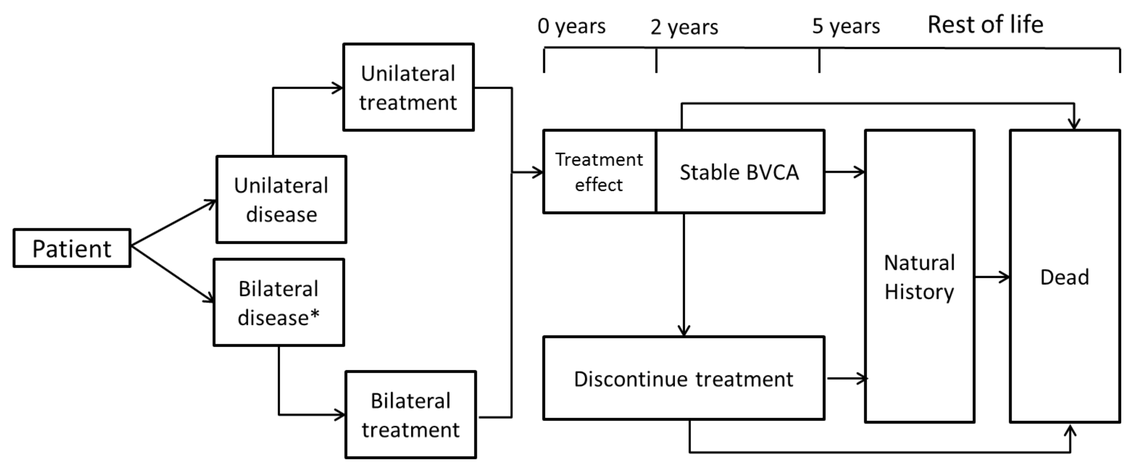
Figure 1: Model Diagram



*Note patients can develop Bilateral disease at any time.

Results

Three scenarios based on different ranibizumab treatment and monitoring schedules were analysed (PRN, treat and extend, monitor and extend) in accordance with the revised label.

Consistent with the vision changes observed in the IVAN trial, the model predicted a very slight treatment benefit in favour of ranibizumab. For both treatments moderate increases in BCVA were observed in the first 3 months of treatment followed by a gradual decline, such that at 24 months vision was similar to that at baseline.

Lifetime costs were lower for ranibizumab than for aflibercept in all three scenarios. The number of total discounted QALYs was also very similar between the two arms. Ranibizumab was associated with 5.073 total QALYs and aflibercept was associated with 5.071 total QALYs. As ranibizumab led to greater health gains at lower cost in all three scenarios, it was dominant compared with aflibercept.

In all three scenarios, the model was most sensitive to the administration costs for ranibizumab and aflibercept; with higher administration costs for ranibizumab and lower administration costs for aflibercept associated with increasing NMB.

Probabilistic sensitivity analysis suggests that ranibizumab has an 84%, 92% and 30% probability of being cost-effective compared with aflibercept, in the PRN, M&E and T&E scenarios respectively, at a WTP threshold of £20,000 per QALY.

Table 1: Results

Scenario	Ranibizumab total costs	Aflibercept total costs	Ranibizumab total QALYs	Aflibercept total QALYs	ICER
PRN	£30,780	£34,644	5.073	5.071	Dominant
M&E	£29,946	£34,644	5.073	5.071	Dominant
T&E	£31,837	£34,644	5.073	5.071	Dominant

Conclusions

This was the first study to evaluate the cost-effectiveness of ranibizumab compared with aflibercept for the treatment of patients with nAMD that reflects the latest posology for ranibizumab.

Ranibizumab and aflibercept have been demonstrated to have similar health outcomes, with ranibizumab associated with a gain of 0.002 QALYs. In all three of the ranibizumab posologies tested, total costs were lower than the aflibercept regimen. Consequently, ranibizumab dominated aflibercept regardless of the posology used.

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