Introduction

Geographic Atrophy (GA) is a retinal disease that affects eight million people worldwide. It is prevalent in elderly in developed countries. The disease is slow progressive. Without intervention, many GA patients may eventually develop severe visual loss and go blind in their lifetime. Despite several natural history studies, the long-term disease burden and potential benefits of treating GA remain unclear.

The aim of this work was to simulate the long-term impact of GA on visual disability and blindness, and the expected benefits of intervention. A micro-simulation model was developed using Excel Visual Basic Application (VBA) to forecast: 1) the long-term risk of becoming visually disabled and blind among subjects with diagnosed GA and 2) the impact of treating GA with a hypothetical intervention.

Methodology

Model Structure:

A micro-simulation model was developed using available natural history data on rate of vision loss among subjects with diagnosed GA. Subjects’ health states were characterized based on visual acuity (VA) in the better-seeing eye as follows:

- No visual disability defined as VA ≥ 54 letters on ETDRS chart (Snellen equivalent: ≥20/80)
- Visual disability defined as VA 36-54 letters on ETDRS chart (Snellen equivalent: ≥20/80 - <20/200)
- Blindness defined as VA ≤ 35 letters on ETDRS chart (Snellen equivalent: <20/200)
- Death

Subjects with GA progress through the visual health states following the rate of VA decline per year as per AREDS report 26. The subjects can encounter death during any one of the visual health states. Time horizon of the model is lifetime.

Model Inputs:

- Lifetime years spent with visual disability (VA ≥ 54 letters)
- Years with blindness (VA ≤ 20/200)
- Years with visual disability and blindness
- Time to event curves for visual disability and blindness
- Treatment (50% efficacy)
- Basecase

Limitations:

- The simulation model captures expected benefit of treatment in terms of reduction in visual disability. The future model will incorporate the health state utilities and costs associated with visual states to model the quality adjusted life year gains and cost effectiveness of intervention.
- The current model simulated the disease burden based on VA better-seeing eye (i.e. worst case scenario). Distribution of visual loss at the eye level in GA subjects needs to be better understood and incorporated into the future model.

Results

The simulation model estimated that without treatment, subjects with GA on average spend four years with visual disability and eight years with blindness during their lifetime.

Without treatment, estimated 91.8% of subjects develop visual disability by year 10 after diagnosis.

- Given a hypothetical treatment with efficacy of 50%, approximately 77.6% of subjects develop visual disability by year 10 (Figure 1a).

Conclusions

The simulation model based on natural history of GA progression showed that GA would cause significant burden in terms of visual disability and blindness and effective treatment can reduce that burden. For subjects under treatment, the reduction in years of blindness improves at an increasing rate in treatment efficacy.

Simulation model is a useful approach to quantify the disease burden and benefits of intervention and aids in addressing unmet medical needs and drug development.

References


Acknowledgement

Many other people have provided valuable input and reviewed at different stage of this work. They are Michael Fries, Gang Chen, Michael Schwarz, Michael Offit, Megan McLaughlin, John Wolterman, Paco Lopez, Shawn Shears. We would like to thank them for the contribution.