A New Patient-Focused Progression Model for Geographic Atrophy

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CONCLUSIONS

- Our model helps translate clinical gains from successfully slowing GA lesion growth into a more practical estimate of the impact on patients' vision-related quality of life (VRQOL) and ultimately a measure of health gain.
- Across all available estimates of clinical efficacy, pegcetacoplan has the potential to have a significant impact on patient health gains in a previously untreatable condition based on phase 2 data.
- Although GA lesion growth slows upon entering the fovea, impact on VRQOL increases. As such, mirroring findings elsewhere,[7] the net health gains are maximized when treatment is begun early, ideally when the lesion is outside of the fovea.

INTRODUCTION

- Geographic atrophy (GA) can cause irreversible blindness. Lesion growth is often used as an endpoint in GA trials. However, studies have not shown strong correlations between total lesion growth and vision[1] or health-related quality of life.
- GA is a complex disease that combines faster lesion growth in the initial stages with slower, but more impactful, growth in later stages.[3] A disease progression model incorporating lesion growth, foveal involvement and the resulting impact on visual acuity (VA) and health-related quality of life (HRQOL), would be more reflective of the value to patients of future GA treatments.

FIGURE 1. Model Structure

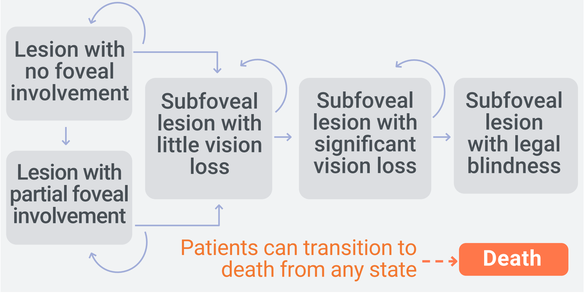


TABLE 1. Inputs for the HSTM

Patient characteristics	Base value	Source
Patient age at baseline	78	Liao et al (2020)[4]
Percent male	40.0%	
STARTING STATE		
NSF >250 microns	25.0%	Khan et al (2021)[5]
NSF 1-249 microns	25.0%	
SF ≤20/40	25.0%	
20/40 < SF <20/200	17.0%	
SF ≥20/200	8.0%	
UTILITIES		
NSF >250 microns	0.84	Claxton et al (2014)[6]
NSF 1-249 microns	0.82	
SF ≤20/40	0.80	
20/40 < SF <20/200	0.67	
SF ≥20/200	0.53	

[**Note**: utility weights assume 57% of treated BSE and 43% WSE; SF: Subfoveal; NSF: Non-subfoveal]

METHODS

- We built a health state transition model (HSTM) to estimate progression of disease in GA patients. Patients move between five states; two where the lesion grows outside the fovea, and three where the lesion grows inside the fovea impacting on visual acuity and VRQOL.
- The model relies on two sources: a real-world analysis of GA patients from the IRIS Registry (N=69,441)[5] and the Sham control arm of a recent phase 2 trial in GA patients.[4] **(Table 1 & 2)**
- The model assumes progression across five states of severity of GA from lesion with no foveal involvement (>250 microns from fovea); lesion with partial foveal involvement (1-249 microns from fovea); lesion entering the subfoveal space with partial vision loss (≤20/40 Snellen score), subfoveal involvement with significant vision loss (between 20/40 and 20/200) and then finally a state of legally blind (≥20/200) using as a terminal state in the model. Death is possible from any state. **(Figure 1)**
- The utility scores for each state were derived from combining utility weights by Snellen score from Claxton et al (2014)[6] multiplied by the proportions of patients whose GA lesion was in their best seeing eye (BSE) and those in the worst seeing eye (WSE). **(Table 1)**
- Assumptions are that treatment continues until discontinuation, death or patients reach the terminal state (legal blindness). Discontinuation is estimated at 5% per cycle, all health gains are discounted at 3.5%.

RESULTS

- We used the model to run two separate scenarios using four estimates of clinical efficacy of pegcetacoplan in the treatment of GA; a mixed cohort of patients at varying stages of GA disease representative of the US GA population **(Table 1)** and a population made up solely of patients whose GA lesion had not yet entered the subfoveal space.
- The sources of efficacy were from the Phase II FILLY trial (N=242),[4] and were from relative reduction in GA lesion growth as a result of monthly and every other month (EOM) treatment. The first set were the relative reduction over the full 12 months, and the second set was that of the period 6-12 months. This is of interest as the initial trials have shown that the efficacy of pegcetacoplan may grow significantly after 6 months on treatment.

TABLE 2. Progression Rates for Standard of Care

	NSF >250 microns	NSF 1-249 microns	SF ≤20/40	20/40 < SF <20/200	SF ≥20/200
NSF >250 microns	70.0%	10.0%	5.0%	15.0%	0.0%
NSF 1-249 microns	0.0%	22.2%	22.2%	55.6%	0.0%
SF ≤20/40	0.0%	0.0%	55.6%	44.4%	0.0%
20/40 < SF <20/200	0.0%	0.0%	4.8%	76.2%	19.0%
SF ≥20/200	0.0%	0.0%	0.0%	0.0%	100.0%

Source: FILLY trial data (Liao 2020)[4], Sham control group. [**Note**: SF: Subfoveal; NSF: Non-subfoveal.]

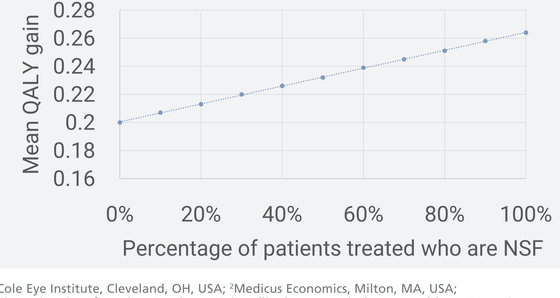
TABLE 3. Efficacy Rates and Results

Source	Efficacy*	Mean QALYs gained per patient** Cohort 1	Cohort 2
FILLY 0-12 MONTHS			
Monthly	29%	0.239	0.264
EOM	20%	0.158	0.175
FILLY 6-12 MONTHS			
Monthly	45%	0.402	0.442
EOM	33%	0.277	0.306

[**Note**: SF: Subfoveal; NSF: Non-subfoveal.] *Relative risk reduction in GA lesion growth. **Cohort 1 assumes all patients treated irrespective of stage of disease. Cohort 2 assumes only NSF patients are treated.

- If all patients across the representative cohort of GA patients are treated with pegcetacoplan then the mean quality-adjusted life year (QALY) gains are between 0.158-0.402 per patient. If limited solely to patients whose lesion is detected before it enters the subfoveal space, the mean QALY gain rises to 0.175-0.442 per patient. **(Table 3)**
- **Figure 2** shows the impact on QALY gain if patients are treated earlier in the course of the disease: it plots the mean QALY gain per patient against the proportion of patients treated whose GA lesion is outside of the subfoveal space at the start of treatment, using the example of clinical efficacy of 29% (FILLY monthly treatment 0-12 months).

FIGURE 2. Percentage NSF to QALYs Gained



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