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A De Novo Cost-Effectiveness Model to Evaluate the Real-World Value of Pegcetacoplan in the Treatment of Geographic Atrophy Secondary to Age-Related Macular Degeneration in the United States

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Introduction

- Geographic atrophy (GA) is a degenerative retinal disease affecting up to an estimated 5 million individuals worldwide,[1] defined by growing atrophic lesions of the outer retina and characterized by progressive and irreversible central vision loss[2]
- In phase 3 trials conducted among patients with GA secondary to age-related macular degeneration (AMD), patients treated with intravitreal pegcetacoplan experienced reduced lesion growth, the primary measure of disease progression,[2] over 30 months relative to patients in the trials' sham control arms[3]

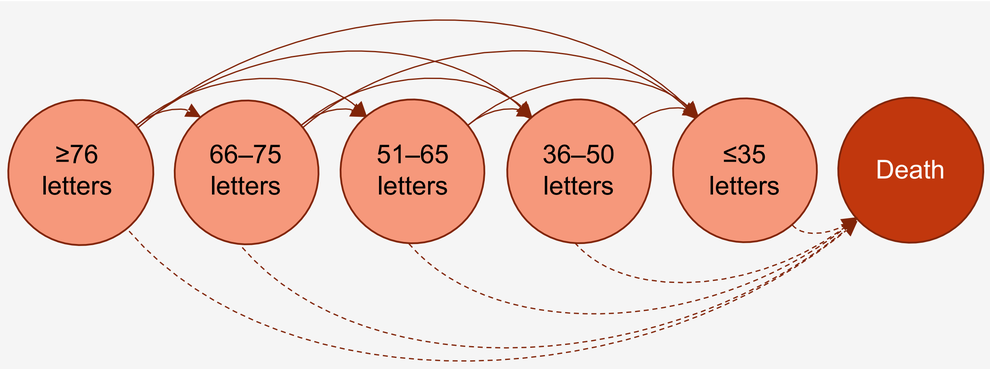
Objective

We developed a health-state transition model to assess the cost effectiveness of pegcetacoplan in 2 US populations: patients with GA secondary to AMD and good or reasonable vision ("all GA"), and the subpopulation of patients whose GA lesions had not yet entered subfoveal space, ie, are extrafoveal ("EF GA"), defined as patients whose GA lesions were ≥250 µm from the foveal center

Methods

- We built a Markov cohort model to estimate average 20-year costs and quality-adjusted life-years (QALYs) accrued per patient from a societal perspective for 2 treatment arms: standard of care (SOC, ie, no treatment) and pegcetacoplan initiated at model time 0
- Consistent with prior studies,[4,5] 5 health states representing progressively worse stages of disease were defined based on best-corrected visual acuity measured in letters (**Figure 1**). Because vision loss attributed to GA is irreversible, transitions to earlier stages of disease (ie, to states with more letters) were not permitted. Transitions to a sixth state—death—were permitted from all states, with likelihoods based on age- and sex-specific 2020 US life tables[6]

Figure 1. Model Structure



- 3-month transition probabilities for SOC were estimated using data from the sham control arm of the DERBY and OAKS clinical trials (**Table 1**).[7] Lesion growth percent reductions with pegcetacoplan vs sham from the GALE trial (Months 1–6: 13%; Months 7–18: 18%; Months ≥19: 33%) were assumed to approximate percent reductions in likelihood of disease progression with pegcetacoplan vs SOC and were applied to the transition probabilities for SOC to obtain time-varying transition probabilities for patients receiving pegcetacoplan[3]

Table 1. 3-Month Disease-Stage Transition Probabilities, SOC

(A) All GA

	≥76 letters	66–75 letters	51–65 letters	36–50 letters	≤35 letters
≥76 letters	80.5%	17.1%	2.0%	0.3%	0.0%
66–75 letters	0.0%	76.9%	21.9%	0.8%	0.5%
51–65 letters	0.0%	0.0%	83.9%	13.3%	2.7%
36–50 letters	0.0%	0.0%	0.0%	79.1%	20.9%
≤35 letters	0.0%	0.0%	0.0%	0.0%	100.0%

(B) EF GA

	≥76 letters	66–75 letters	51–65 letters	36–50 letters	≤35 letters
≥76 letters	85.5%	13.2%	1.3%	0.0%	0.0%
66–75 letters	0.0%	74.7%	25.3%	0.0%	0.0%
51–65 letters	0.0%	0.0%	92.9%	3.6%	3.6%
36–50 letters	0.0%	0.0%	0.0%	53.8%	46.2%
≤35 letters	0.0%	0.0%	0.0%	0.0%	100.0%

Transition probabilities are conditional on survival.
GA, geographic atrophy; **EF,** extrafoveal; **SOC,** standard of care.

- Average annual direct cost of treatment with pegcetacoplan was estimated assuming an average of 7 injections per year priced at $2190 per injection excluding cost of administration. Treated patients were assumed to initiate treatment with pegcetacoplan at model time 0 and discontinue upon reaching the fifth health state representing the lowest level of visual acuity (≤35 letters) and the latest stage of disease
- Other model input values were sourced from additional analyses of DERBY and OAKS trial data, published literature, and publicly available databases (**Table 2**). All costs (2022 USD) and QALYs were discounted at 3% annually

Table 2. Base-Case Input Values

		All GA	EF GA	References
Baseline patient demographics	Age, mean, years	74	72	7, 8
	Male	42%		8
Baseline patient distribution by disease stage	≥76 letters	28%	44%	7, 9
	66–75 letters	29%	34%	
	51–65 letters	39%	19%	
	36–50 letters	3%	3%	
Annual incidence of eAMD	Pegcetacoplan	4%		7
	SOC	2%		
Base utility	≥76 letters	0.82	0.82	7, 10
	66–75 letters	0.75	0.73	
	51–65 letters	0.69	0.66	
	36–50 letters	0.63	0.59	
	≤35 letters	0.56	0.50	
Disutility	Pegcetacoplan injection	-0.0009		11
	Annual caregiver[a]	-0.04		12
Excess annual disease-related HC costs[b]	51–65 letters	7792		13, 14
	36–50 letters	11,140		
	≤35 letters	16,368		
Annual AE-related costs	eAMD[c]	1490		15, 16
Annual indirect caregiver costs	66–75 letters	889		17–19
	51–65 letters	4056		
	36–50 letters	15,871		
	≤35 letters	52,682		

[a]Applied only to patients with ≤65 letters. [b]Reflects difference in mean HC costs for patients with and without vision loss, estimated separately for patients with differing degrees of vision loss. [c]Each patient with incident eAMD was assumed to incur AE-related costs for 4 years upon development of eAMD.
AE, adverse event; **eAMD,** exudative age-related macular degeneration; **EF,** extrafoveal; **GA,** geographic atrophy; **HC,** health care; **SOC,** standard of care.

Results

- We ran the model for both all-GA patients, and for a subgroup of patients whose GA lesions had not yet entered the subfoveal space. In the all-GA population, average costs incurred per patient treated with pegcetacoplan were $8114 higher than those incurred among untreated patients (**Table 3**). Although treated patients sustained greater treatment-related and adverse event (AE)-related direct health care costs, these were largely offset by reduced direct disease-related health care and indirect caregiver costs relative to SOC

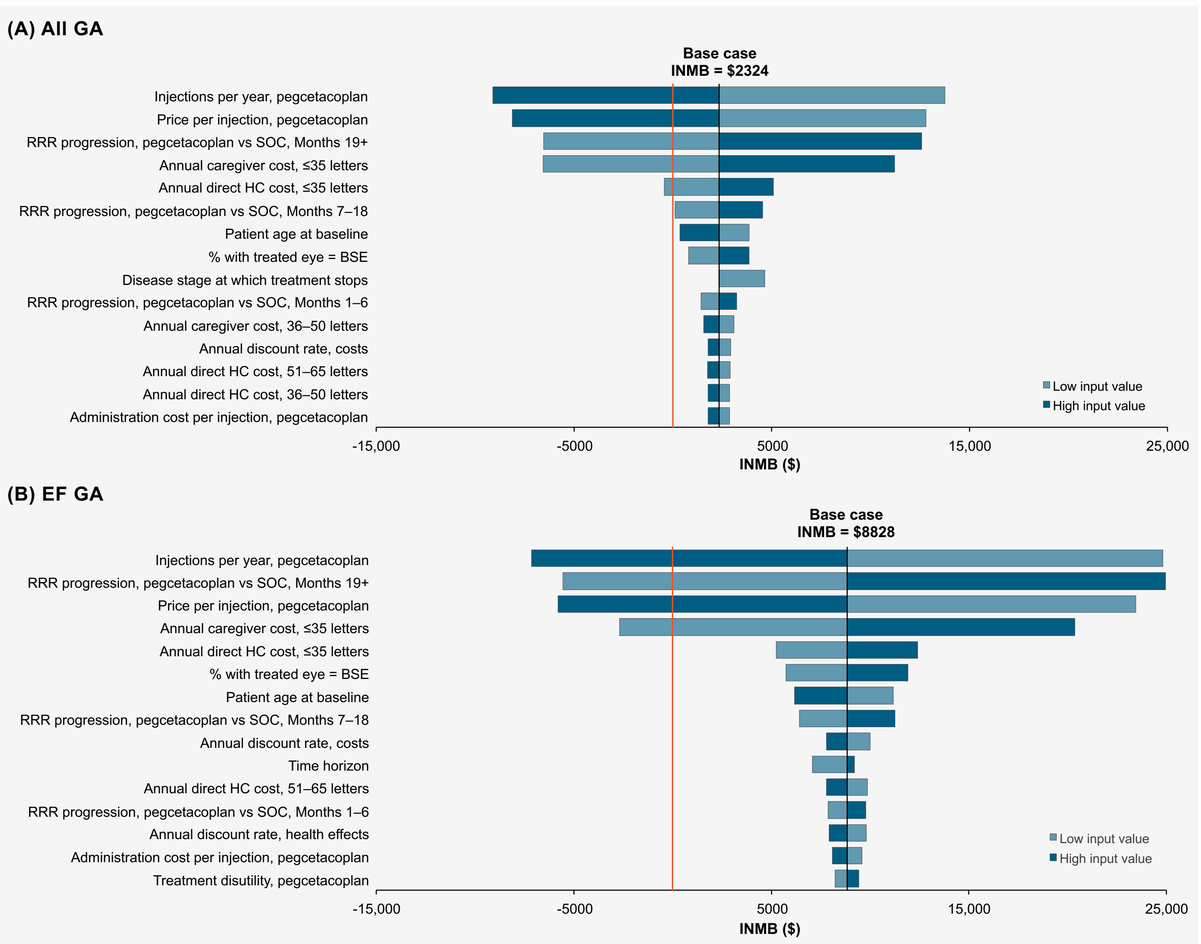
Table 3. Total Average 20-Year Costs and QALYs per Patient

	All GA			EF GA		
	Pegcetacoplan [A]	SOC [B]	Difference [A] - [B]	Pegcetacoplan [C]	SOC [D]	Difference [C] - [D]
Total costs, $	521,625	513,511	8114	485,900	474,752	11,148
Treatment related	54,991	0	54,991	76,923	0	76,923
Disease-related HC	123,013	131,230	-8217	113,683	125,834	-12,151
AE-related HC	1167	898	270	1322	964	358
Indirect caregiver	342,455	381,384	-38,929	293,973	347,954	-53,981
Total QALYs	5.584	5.480	0.104	5.769	5.569	0.200
INMB at $100K/QALY	36,788	34,464	2324	90,957	82,129	8828

AE, adverse event; **EF,** extrafoveal; **GA,** geographic atrophy; **HC,** health care; **INMB,** incremental net monetary benefit; **QALY,** quality-adjusted life year; **SOC,** standard of care.

- Average QALYs accrued per patient in the all-GA population were also higher for those receiving pegcetacoplan relative to SOC (5.584 vs 5.480), attributable to delayed progression to more advanced stages of disease characterized by greater vision loss and lower utility
- These differences in costs and QALYs resulted in an incremental cost-effectiveness ratio (ICER) for pegcetacoplan vs SOC of $77,735 per QALY gained among all-GA patients. Given a maximum willingness to pay (WTP) of $100,000 per QALY in the US, this equates to a positive incremental net monetary benefit (INMB) of $2324 associated with pegcetacoplan
- Similar trends were observed for the EF-GA population but to larger degrees. Because the baseline distribution of EF-GA patients reflects higher proportions of patients in the less severe stages of disease relative to patients in the all-GA population, treated patients in the EF-GA population remained on treatment longer and benefitted more greatly in terms of QALYs gained. As a result, pegcetacoplan was associated with an ICER of $55,806 per QALY and an average INMB of $8828 per patient relative to SOC
- Deterministic sensitivity analyses in which the values of key input parameters were varied in sequence to ±20% of their base-case values indicated that results were most sensitive to number of pegcetacoplan injections per year, price per injection, long-term clinical efficacy, and annual caregiver costs for patients in the most severe stage of disease (**Figure 2**)

Figure 2. Influence of Individual Parameters on INMB: Pegcetacoplan vs SOC



BSE, better-seeing eye; **EF,** extrafoveal; **GA,** geographic atrophy; **HC,** health care; **INMB,** incremental net monetary benefit; **RRR,** relative risk reduction; **SOC,** standard of care.

- However, results from probabilistic sensitivity analyses in which the values of key input parameters were varied simultaneously based on defined distributions were consistent with the base-case results, showing pegcetacoplan is likely to be cost effective at a maximum WTP of $100,000 per QALY (**Figure 3**)

Figure 3. Cost-Effectiveness Acceptability Curves: Pegcetacoplan vs SOC

EF, extrafoveal; **GA,** geographic atrophy; **QALY,** quality-adjusted life year; **SOC,** standard of care; **WTP,** willingness to pay.

Conclusions and Limitations

- Our model suggests pegcetacoplan may be a cost-effective means to slow disease progression and delay blindness in patients with GA
- Early treatment with pegcetacoplan in patients whose lesions have not yet neared the foveal center may provide the most value, although patients at varying stages of disease are likely to benefit
- Due to limitations of trial design, our model necessarily uses data on relative reductions in lesion growth for pegcetacoplan vs sham as proxies for relative reductions in likelihood of disease progression in terms of worsening visual acuity. The model also assumes 7 injection per year for each patient, a mean that represents a wide range. Additionally, it relies on state-specific utility values generated using EuroQoL-5D (EQ-5D) as recommended by current guidelines. However, evidence suggests EQ-5D may be an ineffective tool for measuring vision-related quality of life among patients with AMD[20]
- Additional research is needed to more accurately quantify health-related quality of life at different levels of visual acuity and the associated value of delayed disease progression with treatment in patients with GA

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Disclosures

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