Cost-Effectiveness Analysis of Atogepant in Episodic Migraine Prophylaxis

EE257

Bella Vo, PharmD Candidate, University of Washington School of Pharmacy; David Veenstra, PharmD, PhD

Background

- Episodic migraine (EM) is defined as having a migraine on fewer than 15 days per month. Episodic migraine can progress to chronic migraine and impose a substantial cost burden in the United States.[1,3]
- The American Academy of Neurology recommends preventative therapies for people who experience 4+ monthly migraine days (MMD) and overuse acute medication, or who have headache-related disability.[4]
- The two oral calcitonin gene-related peptide (CGRP) inhibitors, QULIPTA (atogepant) and NURTEC (rimegepant), were approved by FDA for prevention of episodic migraine (EM) in adults.
- Uncertainties remain regarding the effectiveness of atogepant compared with rimegepant, and how well the cost of atogepant will align with patient benefits.

Objective and Method

- The objective of the study was to estimate the incremental cost-effectiveness of atogepant compared to rimegepant in adults with episodic migraine prophylaxis.
- A cost-effectiveness analysis was based on a 3 state Markov model (Figure 1). Cycle length was 4 weeks. The time horizon considered was 2 years. Costs were estimated from societal perspective (including direct costs and productivity costs). A discount rate of 3% was applied to both costs and benefits. All costs were stated as 2022 U.S. dollars. Population included adults with EMs who are candidates for preventative treatment and have not failed more than 2 alternative treatments.
- The treatment effects for atogepant and rimegepant were estimated in terms of migraine days per month and were based on results of two randomized, double-blinded, placebo-controlled trials of each regimen in migraine prophylaxis.[5,6] Migraine baseline in atogepant trial was 7.3 migraine days per month, while the baseline in rimegepant trial was 10.3 migraine days per month.
- Data on costs and health-related quality of life were derived from relevant literatures. The analysis included the following costs: drug cost, adverse event, acute medications, direct healthcare cost, and productivity cost.
- Utilities were derived using EQ-5D-3L data from Johnston et al., 2021. Utility values of on and off atogepant are assumed to be the same with rimegepant since there are no data for all CGRP inhibitors. Disutility from AEs was assumed to be minimal and was not included in the analysis.
- The model assumes that treatment effects and discontinuation rates were constant over the entire model time horizon due to lack of data on long-term treatment effects and discontinuation rates.

Model structure

Figure 1: Markov model diagram of atogepant and rimegepant for preventative treatment of episodic migraine

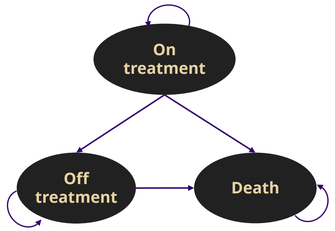


Table 1: Base case model cohort characteristics

Characteristic	Value
Mean age	42.5
Female	86%
Race/Ethnicity	White 83%, Black 12%

Table 2: Model Inputs

Inputs	Mean	Source
Atogepant MMD baseline (days)	7.3	Alani et al., 2021
Atogepant MMD in 4-week period (days)	3.9	Schwet et al., 2022
Rimegepant MMD baseline (days)	10.3	Croop et al., 2020
Rimegepant MMD in 4-week period (days)	7.4	Croop et al., 2020
Utility of on treatment	0.77	Johnston et al.,2021
Utility of off treatment	0.65	Johnston et al.,2021
Cost Inputs (2022 U.S$)		
Atogepant drug cost	$991	WAC Redbook*
Rimegepant drug cost	$1723.6	WAC Redbook*
Physician visit	$112.5	CMS
Hospitalization	$2892.9	CMS
ED visit	$606	CMS
Acute medication	$73.3	Stokes et al. 2011
Atogepant AE cost	$44.4	Estimate
Rimegepant AE cost	$29.8	Estimate
Absenteeism hour cost	$28.98	Estimate
Presenteeism hour cost	$14.49	Estimate

MMD = monthly migrain day; ED = emergency department; AE = adverse event; CMS = Centers for Medicare and Medicaid Services; *Atogepant 60 mg once daily, rimegepant 75 mg every other day

Results

Base-case analysis

Atogepant results in lower total costs ($38,962) compared to rimegepant ($64,559) and higher QALYs (17.11) compared to rimegepant (17.03) in episodic migraine (Table 3).

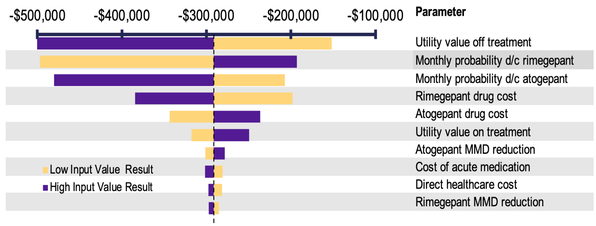
Table 3: Results of base-case analysis

Effectiveness	QALYs (discounted)
Atogepant	17.11
Rimegepant	17.03
Difference	**0.08**
Cost	**Total cost (discounted)**
Atogepant	$38,962
Rimegepant	$64,559
Difference	**$-25,597**

One-way sensitivity analysis

- One-way sensitivity analysis was conducted to identify the key drivers of model outcomes using available measures of parameter uncertainty or reasonable ranges for each input based on clinical trials or ±20% if range not reported. Estimated range of variables for monthly probability of discontinuation is ±5% due to treatment minimal AEs and high tolerability.
- The model was most sensitive to the utility value of off treatment, the probability of treatment discontinuation, and drug costs.

Figure 2: Tornado diagram



Scenario analysis

Table 4: Results of scenario analysis

Effectiveness	QALYs (discounted)
Atogepant	17.11
Rimegepant	17.03
Difference	0.08
Cost	**Total cost (discounted)**
Atogepant	$38,962
Rimegepant	$56,778
Difference	**$-17,816**

- The scenario analysis evaluate the cost and effectiveness of atogepant when patients from both trials were assumed to have the same MMD baseline of 7.3 days.
- Atogepant results in lower total costs $38,962 compared to rimegepant $56,778 and higher QALYs 17.11 compared to rimegepant 17.03 in episodic migraine (Table 4).

Discussion

- The major limitation in this study was the lack of head-to-head comparison between atogepant and rimegepant. The clinical inputs were collected from two clinical trials of each drug compared to the placebo. These two trials have slightly different population. The Rimegepant trial population has a more severe migraine baseline compared to the atogepant trial.
- Another limitation of the study can be found in the estimation of productivity cost. We assumed that the time patients lose because of migraine can be assigned a value corresponding to patients' hourly wage rate. In the real-world, the opportunity cost of lost productivity may be less than gross earnings.
- The 12-week treatment duration is not adequate to assess the long-term safety and side effects of treatments. Long-term real-world studies are needed.
- One-way sensitivity analysis showed that the model was most sensitive to the utility value of off treatment. This result could be due to the wide range of this parameters. This data was solely based on rimegepant trial. The utility value of discontinue atogepant could be different. Future search on the utility of oral CGRP inhibitors would increase the accuracy of the result.

Conclusions

- Preliminary results of this study suggest that atogepant may be dominant compared to rimegepant for episodic migraine prevention from societal perspective.
- Evaluation of real-world effectiveness are needed to clarify the relative effectiveness of these drugs.

References

1. Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. Headache. 2015;55 Suppl 2:103-126. doi:10.1111/head.12505_2
2. Smitherman TA, Burch R, Sheikh H, Loder E. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. Headache. 2013;53(3):427-436. doi:10.1111/head.12074
3. Bonafede M, Sapra S, Shah N, Tepper S, Cappell K, Desai P. Direct and Indirect Healthcare Resource Utilization and Costs Among Migraine Patients in the United States. Headache. 2018;58(5):700-714. doi:10.1111/head.13275
4. Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012;78(17):1337-1345. doi:10.1212/WNL.0b013e3182535d20
5. Ailani J, Lipton RB, Goadsby PJ, et al. Atogepant for the Preventive Treatment of Migraine. N Engl J Med. 2021;385(8):695-706. doi:10.1056/NEJMoa2035908
6. Croop R, Lipton RB, Kudrow D, et al. Oral rimegepant for preventive treatment of migraine: a phase 2/3, randomised, double-blind, placebo-controlled trial. Lancet. 2021;397(10268):51-60. doi:10.1016/S0140-6736(20)32544-7
7. Messali A, Sanderson JC, Blumenfeld AM, et al. Direct and Indirect Costs of Chronic and Episodic Migraine in the United States: A Web-Based Survey. Headache. 2016;56(2):306-322. doi:10.1111/head.12755
8. Centers for Medicare and Medicaid Services. Physician Fee Schedule Search. 2022; https://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx. Accessed Oct 20th, 2022.
9. Johnston KM, L'Italien G, Popoff E, et al. Mapping Migraine-Specific Quality of Life to Health State Utilities in Patients Receiving Rimegepant. Adv Ther. 2021;38(10):5209-5220. doi:10.1007/s12325-021-01897-2
10. Centers for Disease Control and Prevention. United States Life Tables - 2020; https://www.cdc.gov/nchs/data/nvsr/nvsr71/nvsr71-01.pdf. Accessed October 30th, 2022.
11. Schwedt TJ, Lipton RB, Ailani J, et al. Time course of efficacy of atogepant for the preventive treatment of migraine: Results from the randomized, double-blind ADVANCE trial. Cephalalgia. 2022;42(1):3-11. doi:10.1177/03331024211042385