

A Cost Utility Analysis of Zuranolone in the Treatment of Major Depressive Disorder

Kim H, MHS¹; Cheng SY, MHS²; Ballreich J, PhD, MHS²; Levy J, PhD²
¹Department of Practice, Sciences, and Outcomes Research , University of Maryland, Baltimore
²Department of Health Policy & Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Introduction

Zuranolone is an intervention in clinical development for the treatment of MDD and postpartum depression. As a neuroactive steroid, it was developed to overcome the unfavorable side effect profile, dosage schedule, and route of administration of its sister medication brexanolone (Eldar-Lissai et al, 2020).

Methodology

Model structure:

- 1st stage: 2-week decision tree with four outcomes: remission (HAM-D < 7), response without remission (HAM-D score reduction more than 50% from baseline), no response, or dropout.
- 2nd stage: Markov model run in 6- week cycles for a total of 49 weeks.

Intervention: 30mg zuranolone administered daily for a single-14-day cycle.

Comparator: Mirtazapine administered daily.

Population: 29-year-old patients with severe major depressive disorder.

Perspective: US healthcare perspective.

Time horizon: 1 year.

Efficacy-extrapolation: Studied were pooled comparing either intervention to placebo to generate a hypothetical placebo population. A baseline placebo rate for each response type was calculated and the relative risk of each response type in either intervention vs placebo were computed based off comparative statistics using R. Efficacy parameters for zuranolone were extracted from the recent MOUNTAIN trial, SAGE-217, and other phase II and III trials.

Costs: Zuranolone costs were based off its wholesale acquisition cost \$15,900 for a 14-day cycle. Daily mirtazapine treatment was assumed to cost \$4.99 based off US Medicare fee schedules. Annual inpatient, outpatient, ER-related costs, SSRI, and counseling costs were also calculated for each health state. Costs are presented in 2022 USD.

Outcomes: Quality-adjusted life years. Cost effectiveness conclusions were determined off WTP thresholds from \$50,000-\$150,000. Net monetary benefit for each intervention at WTP thresholds of \$50,000 and \$100,000 were also calculated.

Sensitivity analyses: Both deterministic and probabilistic sensitivity analyses were conducted.

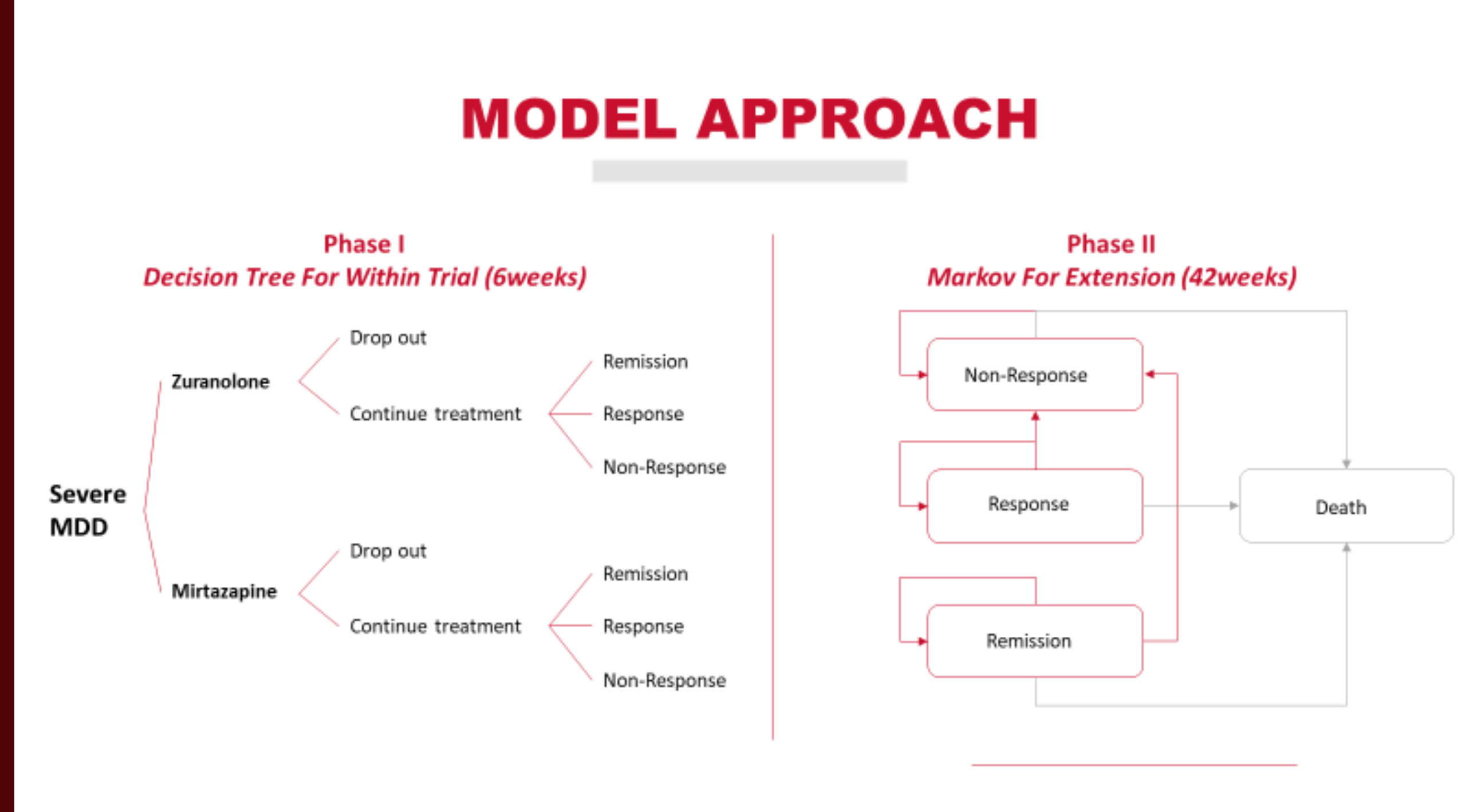
Assumptions:

- 28% and 11% of the zuranolone and mirtazapine cohorts respectively received daily SSRI therapy in line with clinical trial observations.
- Singular remission state and in consequence, a single utility weight for patients in the remission health state.
- Transition probabilities from remission or response without remission to no response based off the STAR*D study.

Inputs

Table 1. Model input parameters				
Parameters	Base Case	Range for DSA	Distribution	Citation
Zuranolone: 14 day course	\$15,900	\$7,500- \$30,000	Log Normal	Eldar-Lissai et al, 2020
Mirtazapine: daily	\$4.99	\$2.7 - \$7.34	Gamma	US Medicare Fee Schedule
SSRI: 6 weeks	\$6.42	\$5.13 - \$7.70	Gamma	Eldar-Lissai et al, 2020
Outpatient: annual costs				
No response	\$8,690.85	\$6,952.68 - \$10,429.02	Gamma	Greenberg et al, 2021
Response without remission	\$6,952.68	\$5,562.144 - \$8,343.22	Gamma	Greenberg et al, 2021
Remission	\$4,523.40	\$3,618.72 - \$5,428.08	Gamma	Bains et al, 2023
Inpatient: annual costs				
No response	\$3,966.90	\$3,173.52 - \$4,760.28	Gamma	Greenberg et al, 2021
Response without remission	\$3,173.52	\$2,538.82 - \$3,808.22	Gamma	Greenberg et al, 2021
Remission	\$1,620.15	\$1,296.12 - \$1,944.18	Gamma	Bains et al, 2023
ER: annual costs				
No response	\$1,184.40	\$947.52 - \$1,421.28	Gamma	Greenberg et al, 2021
Response no remission	\$823.73	\$659.98 - \$988.47	Gamma	Greenberg et al, 2021
Remission	\$549.15	\$439.3 - \$658.98	Gamma	Bains et al, 2023
Counseling: annual	\$2,310.00	\$1,848 - \$2,772	Gamma	Greenberg et al, 2021
Utility				
Baseline	0.410	0.253 - 0.589	Gamma	Puyat et al, 2016
Change: remission	0.120	0.014 - 0.363	Gamma	Ross et al, 2019
Change: response without remission	0.120	0.014 - 0.363	Gamma	Pyne et al, 2009
Change: no response	0.050	0.002 - 0.219	Gamma	Pyne et al, 2009
Transition Probabilities (week 0 to 6)				
Zuranolone				
Remission	0.692	0.175 - 0.376	Beta	Cipriani et al, 2018
Response	0.254	0.0224 - 0.198	Beta	Stahl et al, 1997
No response	0.055	0.419 - 0.813	Beta	Cipriani et al, 2018
Mirtazapine				
Remission	0.424	0.35 - 0.64	Beta	Cipriani et al, 2018
Response	0.183	0.05 - 0.51	Beta	Stahl et al, 1997
No response	0.394	0.206 - 0.60	Beta	Cipriani et al, 2018
Transition Probabilities (weeks 6 to 48)				
Remission to no response	0.046	0.04 - 0.08	Beta	Penninx et al, 1999
Response without remission to no response	0.097	0.08 - 0.19	Beta	Questions, 2023
Remission to death	0.005	0.003 - 0.006	Beta	Penninx et al, 1999
Response without remission to death	0.008	0.006 - 0.013	Beta	Questions, 2023
No response to death	0.007	0.006 - 0.008	Beta	Penninx et al, 1999

Figure 1. 2-part model structure



References

Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., Leucht, S., Ruhe, H. G., Turner, E. H., Higgins, J. P. T., Egger, M., Takeshima, N., Hayasaka, Y., Imai, H., Shinohara, K., Tajika, A., Ioannidis, J. P. A., & Geddes, J. R. (2018). Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: A systematic review and network meta-analysis. *Lancet* (London, England), 391(10128), 1357–1366. [https://doi.org/10.1016/S0140-6736\(17\)32802-7](https://doi.org/10.1016/S0140-6736(17)32802-7)

Bains, N., & Abdjadjid, S. (2023). Major Depressive Disorder. In StatPearls. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK653078/>

Eldar-Lissai, A., Cohen, J. T., Meltzer-Brody, S., Gerbasi, M. E., Chertavian, E., Hodgkins, P., Bond, J. C., & Johnson, S. J. (2020). Cost-Effectiveness of Brexanolone Versus Selective Serotonin Reuptake Inhibitors for the Treatment of Postpartum Depression in the United States. *Journal of Managed Care & Specialty Pharmacy*, 26(6), 627–638. <https://doi.org/10.1895/jcsm.2019.1533>

Penninx, B. W. J. H., Geerlings, S. W., Deeg, D. J. H., van Eijk, J. T. M., van Tilburg, W., & Beekman, A. T. F. (1999). Minor and Major Depression and the Risk of Death in Older Persons. *Archives of General Psychiatry*, 56(10), 889–895. <https://doi.org/10.1001/archpsyc.56.10.889>

Puyat, J. H., Kazanjian, A., Goldnes, E. M., & Wong, H. (2016). How Often Do Individuals with Major Depression Receive Minimally Adequate Treatment? A Population-Based, Data Linkage Study. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, 61(7), 394–404. <https://doi.org/10.1177/0706437116642288>

Pyne, J. M., Fortney, J. C., Tipathji, S., Feeny, D., Ubel, P., & Brazier, J. (2009). How Bad Is Depression? Preference Score Estimates from Depressed Patients and the General Population. *Health Services Research*, 44(4), 1406–1423. <https://doi.org/10.1111/j.1475-6753.2009.00974.x>

Results

Table 2. Base case results after 1 year

Intervention	Costs per Patient	QALYs per Patient	Incremental Costs per Patient	Incremental QALYs per Patient	ICER	NMB 50K	NMB 100K
Zuranolone	\$22,236	0.56	\$12,520	0.043	\$287,441	\$5,741	\$33,717
Mirtazapine	\$9,716	0.52	-	-	-	\$16,083	\$41,881

Figure 2. Results of 1,000 iterations of probabilistic sensitivity analyses: Cost effectiveness acceptability curve



- The one-year costs and QALYs of zuranolone were \$22,236 and 0.56 per patient and \$9,716 and 0.52 per patient for mirtazapine, for an ICER of \$287,442.
- Results were most sensitive to drug cost, relative risk of remission, and remission health-state utility. In sensitivity analyses, zuranolone was the preferred treatment in 15% of the total draws under a willingness to pay threshold of \$100,000.
- The Zuranolone cohort incurred most of its costs in the first part of the model with cost savings observed in the Markov model due to the single 14-day-treatment-cycle strategy.
- The Mirtazapine cohort incurred most its costs in the second part of the model.
- 69% and 42% of the patients in the Zuranolone and Mirtazapine respectively reached remission in the first stage, followed by 37% and 23% in the second stage.

Conclusions

Zuranolone’s biggest appeal come from its short use and the potentially sustained effect over 6 months to a year. Treatment duration has significant implications on patient adherence to MDD medication, which is one of the main drivers for improved health outcomes in this disease space. However, given its efficacy profile in MDD patients according to the MOUNTAIN trial, zuranolone’s current price should reflect a balance between its short-use duration and treatment efficacy.