Cost-Effectiveness of Delaying Progression of Alzheimer's Disease with Novel Monoclonal Antibodies: A Societal Perspective

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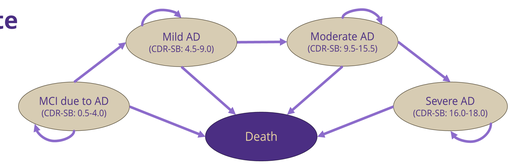
Background

- Since 2021, the FDA has approved three monoclonal antibodies (mAbs) that have demonstrated efficacy in reducing beta-amyloid plaques and improving clinical symptoms of Alzheimer's Disease (AD).[1,2,3]
- In November 2024, Biogen discontinued manufacturing aducanumab, leaving only lecanemab and donanemab available on the market.
  - Despite several years since the initial introduction of mAbs as an AD treatment, access to these drugs remains uncertain due to high drug-related costs and financial burden[21]
- A cost-effectiveness review of these mAbs is critical to support informed decision-making by healthcare stakeholders and policymakers regarding access of these medications to patients with AD.
- **OBJECTIVE | To evaluate the cost-effectiveness of the novel mAb treatments in delaying AD progression in patients with Mild Cognitive Impairment (MCI)**

Methods

- Cost-effectiveness (CE) model was built using Markov approach (Figure 1), comparing aducanumab, lecanemab, and donanemab with standard of care (SOC)† for AD.
- Drug efficacy and population characteristics were derived from the phase 3 clinical trials.[8,9,10]
  - Population Age: 65 years, Male%: 45.9%, AD severity (CDR-SB): 3.3
- A 1-week cycle length and a 10-year time horizon was used to estimate CE from a societal perspective.
- All analyses were conducted using R (version 4.4.3) and Microsoft Excel.

Figure 1. 5-State Markov Model



Key model assumptions were as follows:

- Progression is unidirectional, and patients do not improve. (*Figure 1*)
- Cost and Utilities are mapped to levels of AD severity in CDR-SB.
- Progression under the mAbs follows a similar trajectory shape as the progression under SOC.[4] (*Figure 2*)
- Once patients reach moderate AD, the treatments were assumed not efficacious and thus discontinued.
- Health state transitions under each treatment are extrapolated based on established estimates. (*Figure 3*)
- All adverse events are assumed to be experienced during the first 6 months of starting the therapies.
- Patients receive the treatments at the recommended maintenance dosing that is approved by FDA.[5,6,7]
- Medicaid cost sharing increases with disease progression at an assumed distribution of coverage.
- Discount were assumed at 3% for cost and outcome.

Supplemental & References

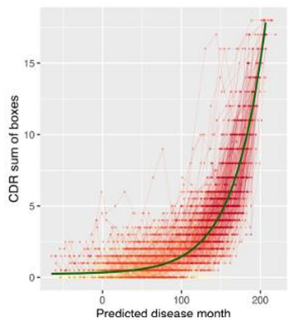


Figure 2. AD Progression Trajectory Curve and Equation Mapped In CDR-SB[4]

$$\mu(t) = l \cdot \exp\left(\frac{t}{\exp(g)}\right) + v$$

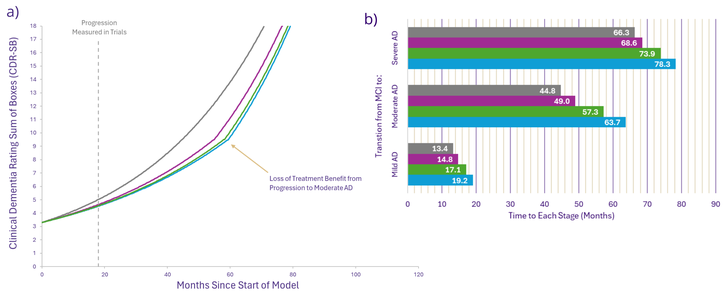
g = scaling of time
v = mean score of cognitively normal individuals
l = mean deviation from v at time t=0

AD: Alzheimer's Disease; mAbs: Monoclonal Antibodies; MCI: Mild Cognitive Impairment; SOC: Standard of Care
†SOC is defined as common treatment regimen in early AD patients including prescriptions like donepezil, memantine, galantamine, rivastigmine, etc.

Results

SOC† | LECANEMAB | ADUCANUMAB | DONANEMAB

Figure 3. a) Projected Progression Curves in CDR-SB and b) Transition Time from MCI to Each AD Stage



- The mAbs were estimated to delay AD progression as little as 1.4 months (Mild AD) to nearly 19 months (Moderate AD) compared to SOC.
- Donanemab was more effective in delaying AD progression than aducanumab or lecanemab.
- Lecanemab was more effective in delaying AD progression than aducanumab.

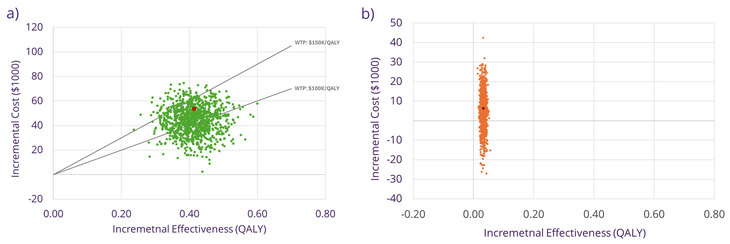
Table 1. Comparative Cost-Effectiveness Results

	Costs	QALY	ICER
SOC	$911,000	3.43	---
Aducanumab	$956,000	3.71	$160,300
Lecanemab	$964,600	3.84	$129,800
Donanemab	$971,100	3.87	$192,600

*All dollars are in 2024 USD

- All treatments generated more costs and QALYs than SOC. Aducanumab was less cost-effective ($160,300) than lecanemab, thus was dominated by lecanemab.

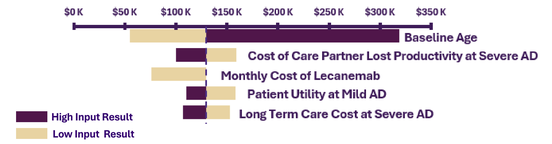
Figure 4. Cost-Effectiveness Scatterplot with 1000 Simulations: a) Lecanemab vs. SOC, b) Donanemab vs. Lecanemab



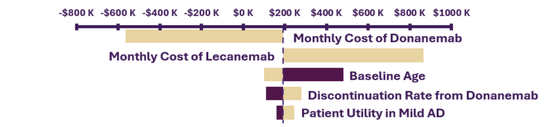
- Lecanemab resulted in higher costs and greater QALY gains compared to SOC, with a 38.8% probability of cost-effectiveness at $100K/QALY and 89.6% at a $150K/QALY.
- Donanemab incurred slightly more QALY gains compared to lecanemab.

Figure 5. One Way Sensitivity Analyses:

a) **Lecanemab vs. SOC**

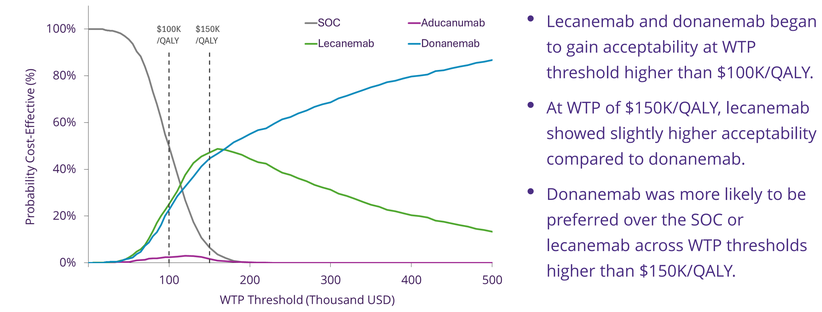


b) **Donanemab vs. Lecanemab**



- The key drivers for cost-effectiveness for lecanemab over SOC were: (1) age that patient initiated the treatment, (2) care partner lost productivity, (3) drug cost and (4) patient utility.
- Treatment costs demonstrated the largest impacts on CE of donanemab over lecanemab.

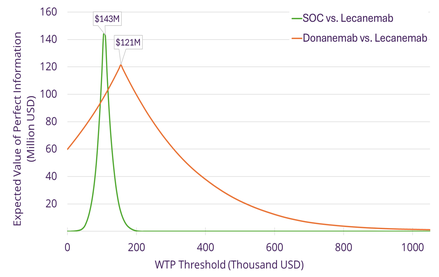
Figure 6. Cost-Effectiveness Acceptability Curve (CEAC)



- Lecanemab and donanemab began to gain acceptability at WTP threshold higher than $100K/QALY.
- At WTP of $150K/QALY, lecanemab showed slightly higher acceptability compared to donanemab.
- Donanemab was more likely to be preferred over the SOC or lecanemab across WTP thresholds higher than $150K/QALY.

Figure 7. Expected Value of Perfect Information (EVPI)

- Additional information may be reasonable to cost up to $143M at a WTP threshold of $150K/QALY to support decisions between SOC and lecanemab.
- The value of additional information to support decisions between lecanemab and donanemab remained lower, peaking at $121M at a WTP threshold of $200K/QALY.



Limitations

- Lack of comparative clinical evidence (i.e. head-to-head trials) makes difficult to demonstrate relative efficacy of the treatments.
- The model assumptions may not accurately reflect the natural progression of the disease or the long-term impact of the treatments.
- 10-year time horizon was used instead of a lifetime time horizon.

Conclusion

- Aducanumab and donanemab is not likely to be cost-effective under the WTP threshold of $150K/QALY.
- Lecanemab is more cost-effective than both aducanumab and donanemab. With aducanumab withdrawn from the market, lecanemab would be favored over donanemab.
- The greater value of information highlights a greater uncertainty in justifying lecanemab over the standard of care and the strong need for further research to support informed decision-making around the novel monoclonal antibodies.