EE632

Early Cost-Effectiveness of SPECTRIS™ Therapy (evoking gamma band oscillations) in Alzheimer's Disease demonstrates favourable annual per patient and health care system cost profile

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Introduction

- Over 6 million Americans live with Alzheimer's disease (AD), costing the U.S. an estimated $321 billion annually, with unpaid caregiving adding another $271 billion[1]. Approved monoclonal antibodies impose a significant additional cost per patient, while facing concerns about clinically meaningful impact.[2]
- Spectris is an investigational non-invasive, at-home AD treatment that delivers visual and auditory stimulation, evoking gamma band oscillations in the brain. Brain gamma frequency oscillations are known to be disrupted in AD patients.[3]
- The Phase II randomized sham controlled, double-blind 6- month trial (RCT), OVERTURE I, demonstrated a 77% reduction in decline of daily function as measured by Alzheimer's Disease Cooperative Study Activities of Daily Living (ADCS-ADL) versus the sham group, with no serious treatment-limiting adverse events.[4]
- The HOPE trial, a 12-month pivotal phase III randomized controlled study, aims to enroll approximately 670 participants to confirm the efficacy and safety of the Spectris device.

Objective

To develop an early-stage cost-effectiveness model that evaluates the economic value of Spectris in mild-moderate AD patients in the U.S under various efficacy scenarios.

Methods

- A five-state Markov model characterizing AD progression was developed to model health-related quality of life (HRQoL) and costs over a lifetime horizon from a US payer perspective (costs and QALYs discounted 3%).

Transition probabilities between alive health states

	MCI due to AD	Mild AD	Moderate AD	Severe AD
MCI due to AD	77%	23%	0%	0%
Mild AD	3%	96.24%	0.68%	0.08%
Moderate AD	0%	3%	96.63%	0.37%
Severe AD	0%	0%	2%	98%

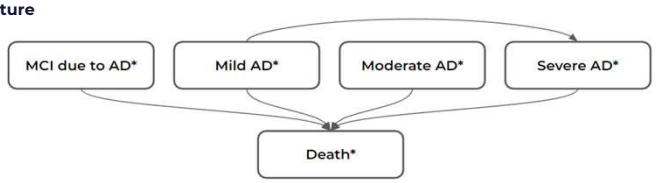
Patient and caregiver utility estimates

	Patient utility		Caregiver utility	
	Community	Long-term care	Community	Long-term care
MCI due to AD	0.73	0.73	0.88	0.88
Mild AD	0.86	0.71	0.86	0.86
Moderate AD	0.54	0.48	0.83†	0.83†
Severe AD	0.37	0.31	0.81†	0.81†

Annual medical costs stratified by disease severity

	65-84 years age group	85+ years age group
MCI due to AD	$76,228.49	$226,987.79
Mild AD	$105,989.08	$315,606.75
Moderate AD	$131,219.98	$390,737.53
Severe AD	$131,219.98	$390,737.53

Model Structure



- All health states were at risk of transitioning to the death state due to all-cause and disease-specific mortality, with a model cycle length of one year
- Specific to each health state, the model also tracked the setting of care (i.e., community or long-term care)
- Patients were able to transition from community to long-term care; however, once in long-term care, they remained there until death
- Individuals remained in the model until they died

Model inputs & parameters

- Spectris was assumed to be used in combination with supportive care (SC). SC transition probabilities, utilities and other cost inputs were identified using published sources. – following ICER report methodology.
- The observed decrease in ADCS-ADL scores from OVERTURE trial was used to cross-walk from ADCS-ADL to Clinical Dementia Rating scale (CDR) –sum of boxes (SB) following Hallikainen et al 2013 [5], to provide the risk ratio of decline versus SC.
- For Spectris, a range of relative risk (RR) efficacy scenarios between 0.3 (approximating the OVERTURE I results, where a 77% reduction in functional decline was observed) and 0.7 (consistent with available monoclonal antibodies) were applied to SC transition probabilities.
- Across this range, a cost-effective acquisition cost of Spectris was calculated at a willingness-to-pay (WTP) threshold of $100,000.
- Two-way sensitivity analyses conducted to assess the range of potential economic outcomes across values of these inputs

Results

- Using the previously described efficacy scenarios and a WTP threshold of $100,000/QALY, Spectris would be considered cost effective at an annual acquisition cost over a range of $44,000 (RR = 0.7) to $108,000 (RR = 0.3)
- Following the efficacy observed by the phase II trial, the early model projected 1 additional life year (LY), and 1.13 quality adjusted life years (QALYs) gained with Spectris
- Incremental costs of Spectris were primarily driven by acquisition costs, with background healthcare costs accounting for <1% of costs.
- Key drivers of results are Spectris efficacy relative to untreated patients, and acquisition cost of Spectris.

Treatment effect vs Spectris cost

Acquisition cost range - Spectris

Efficacy RR Range	$10,000	$20,000	$30,000	$40,000	$50,000	$60,000
0.30	$37,909	$44,159	$50,408	$56,658	$62,908	$69,157
0.35	$38,797	$45,649	$52,502	$59,355	$66,208	$73,061
0.40	$39,610	$47,162	$54,714	$62,266	$69,819	$77,371
0.45	$40,372	$48,743	$57,114	$65,485	$73,856	$82,227
0.50	$41,105	$50,446	$59,787	$69,128	$78,469	$87,810
0.55	$41,835	$52,341	$62,848	$73,354	$83,861	$94,367
0.60	$42,589	$54,521	$66,452	$78,384	$90,315	$102,247
0.65	$43,406	$57,117	$70,828	$84,539	$98,250	$111,961
0.70	$44,338	$60,331	$76,325	$92,318	$108,312	$124,305

Threshold $100,000; Green ICER below threshold; Red ICER above threshold

Conclusions

- Early cost-effectiveness modeling demonstrates that Spectris could be a highly cost-effective treatment for Alzheimer's Disease (AD), derived from efficacy and safety outcomes from the Phase II Overture trial.
- Unlike monoclonal antibodies, Spectris is non-invasive, avoids significant side effects (e.g., ARIA), and has a one-off acquisition cost. Additionally, monoclonal antibodies have a high annual cost (>$25,000) and are reported to have a 0% chance of meeting the ICER cost-effectiveness threshold of $100,000 per QALY.[2]
- The ongoing pivotal HOPE trial aims to confirm Spectris' efficacy and safety in a larger population and with longer-term data. This data will be used to update the early cost-effectiveness model and is anticipated to solidify Spectris' position as a durable, cost-effective AD treatment.

References

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[5] Hallikainen I, et al. 2013. Progression of Alzheimer's disease during a three-year follow-up using the CERAD-NB total score: Kuopio ALSOVA study. Int Psychogeriatr. 25(8):1335-44