The Social Value of Lecanemab for Patients with Early Alzheimer's Disease in Japan

EE723

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BACKGROUND & OBJECTIVES

- Lecanemab is the first approved disease-modified therapy in Japan for patients with mild cognitive impairment (MCI) due to AD or mild AD dementia (AD-D).
- This study aimed to evaluate the societal value and value-based pricing (VBP) of lecanemab in Japan.

METHODS

Overview

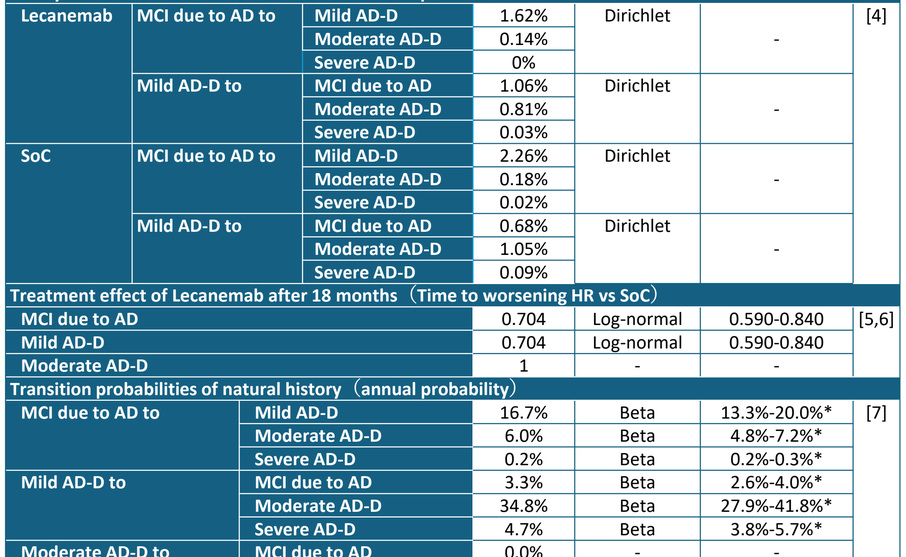
Table 1. Summary of the Study Design

Population	Patients with early AD (MCI due to AD or mild AD-D) with a confirmed Aβ pathology
Intervention	Lecanemab administered every 2 weeks (10 mg/kg) + Standard of care (SoC)
Comparator	SoC
Perspective	Public healthcare and long-term care payers
Time horizon	Lifetime (up to 30 years)
Outcomes	Quality-adjusted life year (QALY) • Sum the absolute values of the utilities for both the caregiver and the patient.
Discount rate	Costs and QALYs were discounted at 2% per year[1]
Scenario analyses	• Perspective - Public healthcare payer - Societal (including the informal care costs) • Approach for caregiver utility - Decrement method: subtract the caregiver's disutility from the patient's utility - Increment method: add the caregiver's utility increment to the patient's utility • Relative efficacy for lecanemab after 18 months - Using HRs estimated from 18-data from Clarity AD (HR: 0.729) - Using HRs estimated from 48-data from Clarity AD (HR: 0.679) • Ages of onset for the target population - 65 years / 75 years • Assuming the introduction of a maintenance dose, changing the dosing frequency from every two weeks to every four weeks after 18 months • Assuming the relative efficacy of lecanemab, persisting up to moderate AD-D

Model structure

- A Markov state transition model, with health states based on disease severity, institutionalization, and death, was developed.

Figure 1. Model structure



Model Input

Table 2. Clinical parameter

Variable			Value	Sensitivity analysis: Distribution	Sensitivity analysis: DSA Setting	Ref
Characteristics						
Starting age (years)			71.46	Gamma	69.95-72.97	[2]
% female			68.1%	Beta	59.6%-76.6%	
Mean weight (kg)			50.0	Gamma	40.0-60.0	[3]
Clarity-AD transition distribution at 0-18 months （per month）						
Lecanemab	MCI due to AD to	Mild AD-D	1.62%	Dirichlet	-	[4]
		Moderate AD-D	0.14%			
		Severe AD-D	0%			
	Mild AD-D to	MCI due to AD	1.06%	Dirichlet	-	
		Moderate AD-D	0.81%			
		Severe AD-D	0.03%			
SoC	MCI due to AD to	Mild AD-D	2.26%	Dirichlet	-	
		Moderate AD-D	0.18%			
		Severe AD-D	0.02%			
	Mild AD-D to	MCI due to AD	0.68%	Dirichlet	-	
		Moderate AD-D	1.05%			
		Severe AD-D	0.09%			
Treatment effect of Lecanemab after 18 months （Time to worsening HR vs SoC）						
MCI due to AD			0.704	Log-normal	0.590-0.840	[5,6]
Mild AD-D			0.704	Log-normal	0.590-0.840	
Moderate AD-D			1	-	-	
Transition probabilities of natural history （annual probability）						
MCI due to AD to	Mild AD-D		16.7%	Beta	13.3%-20.0%*	[7]
	Moderate AD-D		6.0%	Beta	4.8%-7.2%*	
	Severe AD-D		0.2%	Beta	0.2%-0.3%*	
Mild AD-D to	MCI due to AD		3.3%	Beta	2.6%-4.0%*	
	Moderate AD-D		34.8%	Beta	27.9%-41.8%*	
	Severe AD-D		4.7%	Beta	3.8%-5.7%*	
Moderate AD-D to	MCI due to AD		0.0%	-	-	
	Mild AD-D		2.6%	Beta	2.1%-3.1%*	
	Severe AD-D		41.6%	Beta	33.3%-49.9%*	
Severe AD-D to	MCI due to AD		0.0%	-	-	
	Mild AD-D		0.0%	-	-	
	Moderate AD-D		2.4%	Beta	2.0%-2.9%*	
AD specific mortality (HR, vs General population mortality)						
MCI due to AD			1.14	Log-normal	0.91-1.37*	[8]
Mild AD-D			1.55	Log-normal	1.24-1.86*	
Moderate AD-D			2.80	Log-normal	2.24-3.36*	
Severe AD-D			5.48	Log-normal	4.38-6.58*	
Monthly discontinuation rate after 36 month						
Lecanemab	MCI due to AD population		0.9%	Beta	0.7%-1.0%*	[9]
	Mild AD-D population		1.4%	Beta	1.1%-1.7%*	
Transition rate to institutionalization （/18 months）						
MCI due to AD			0.0%	-	-	[10]
Mild AD-D			3.2%	Beta	0.4%-6.0%	
Moderate AD-D			9.1%	Beta	5.2%-13.0%	
Severe AD-D			8.5%	Beta	4.5%-12.5%	

* Set to ±20% of the basic analysis setting value

Declaration of COI

- This work was supported by Eisai Co., Ltd. and Biogen Inc.

METHODS COT.

Table 3. Utilities

Variable	Value	Sensitivity analysis: Distribution	Sensitivity analysis: DSA Setting	Ref
Patient health state utilities				
MCI due to AD	0.880	-	-	[11]
Mild AD-D	0.814	Beta	0.724-0.904	[12]
Moderate AD-D	0.713	Beta	0.672-0.754	
Severe AD-D	0.487	Beta	0.447-0.528	
Utility decrement due to institutionalization				
MCI due to AD, Mild AD-D	0	Normal	-0.11-0.12	[13]
Moderate AD-D, Severe AD-D	0.13	Normal	0.03-0.23	
Caregiver utilities (Base-case analysis)				
MCI due to AD	0.929	-	-	[11]
Mild AD-D	0.911	Beta	0.865-0.956	[14]
Moderate AD-D	0.878	Beta	0.808-0.965	
Severe AD-D	0.858	Beta	0.746-0.987	
Caregiver utility decrement due to institutionalization				
Institutionalization (all severities)	0.050	Beta	-0.03-0.13	[13]
Caregiver utility decrement (Scenario analysis)				
MCI due to AD	0	-	-	[11,
Mild AD-D	0.018	-	-	14]
Moderate AD-D	0.051	-	-	
Severe AD-D	0.071	-	-	
Caregiver utility increment (Scenario analysis)				
MCI due to AD	0.071	-	-	[11,
Mild AD-D	0.053	-	-	13,
Moderate AD-D	0.020	-	-	14]
Severe AD-D	0	-	-	
Community setting	0.050	-	-	

Table 4. Cost parameter

Variable		Value	Sensitivity analysis: Distribution	Sensitivity analysis: DSA Setting	Ref
Lecanemab drug cost					
Lecanemab IV infusion 200mg (JPY)		45,777	-	-	[15]
Lecanemab IV infusion 500mg (JPY)		114,443	-	-	
Compliance rate		94.18%	Beta	75.34%-100.00%*	[9]
Direct medical and long-term care costs (JPY per year)					
Direct medical costs	MCI due to AD	203,495	Gamma	162,796-244,194*	[16]
	Mild AD-D	540,446	Gamma	432,357-648,535*	
	Moderate AD-D	827,059	Gamma	661,647-992,471*	
	Severe AD-D	955,408	Gamma	764,326-1,146,490*	
Community residential care costs	MCI due to AD	171,230	Gamma	136,984-205,476*	
	Mild AD-D	591,363	Gamma	473,090-709,636*	
	Moderate AD-D	1,116,586	Gamma	893,269-1,339,903*	
	Severe AD-D	1,662,994	Gamma	1,330,395-1,995,593*	
Institutional residential care costs	MCI due to AD	409,470	Gamma	327,576-491,364*	
	Mild AD-D	1,580,673	Gamma	1,264,538-1,896,808*	
	Moderate AD-D	2,915,462	Gamma	2,332,370-3,498,554*	
	Severe AD-D	3,498,879	Gamma	2,799,103-4,198,655*	
Informal care cost (JPY per year) (Scenario analysis)					
Community residential care	MCI due to AD	562,248	-	-	[17]
	Mild AD-D	1,612,980	-	-	
	Moderate AD-D	2,682,420	-	-	
	Severe AD-D	3,718,068	-	-	
Institutional residential care		0	-	-	

* Set to ±20% of the basic analysis setting value

RESULTS

- The lecanemab + SoC prolonged the period spent in early AD and shortened the duration of the severe condition.(Figure 2, 3)
- In the base-case, the ICER for lecanemab + SOC was JPY 8.5 million / QALY for the MCI and JPY 7.9 million / QALY for the mild AD-D. (Table 5)
- Societal benefit is likely to be underestimated, since the rates of ARIA are lower in Japanese population than the overall CLARITY AD population.

Figure 2. Patient disposition in different AD severity levels or death over lifetime

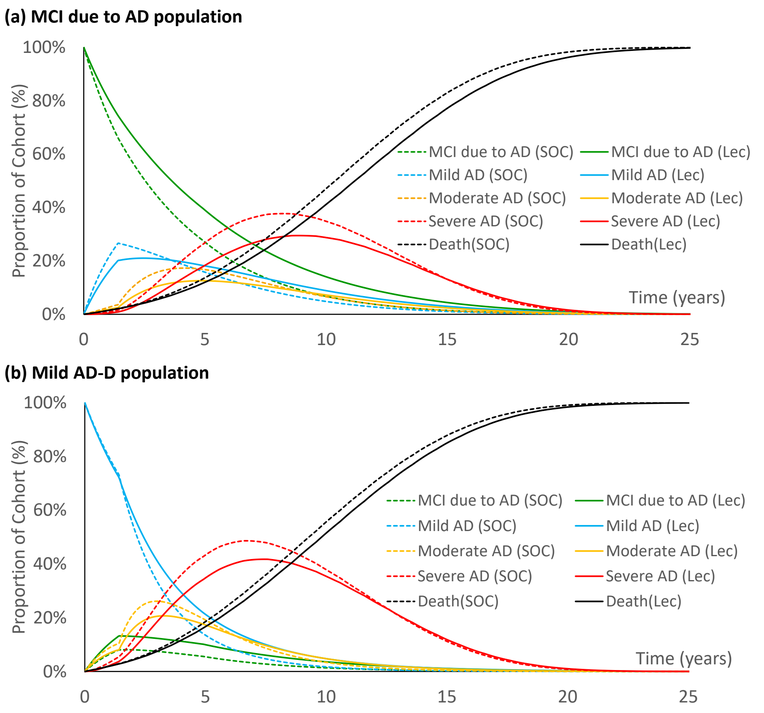
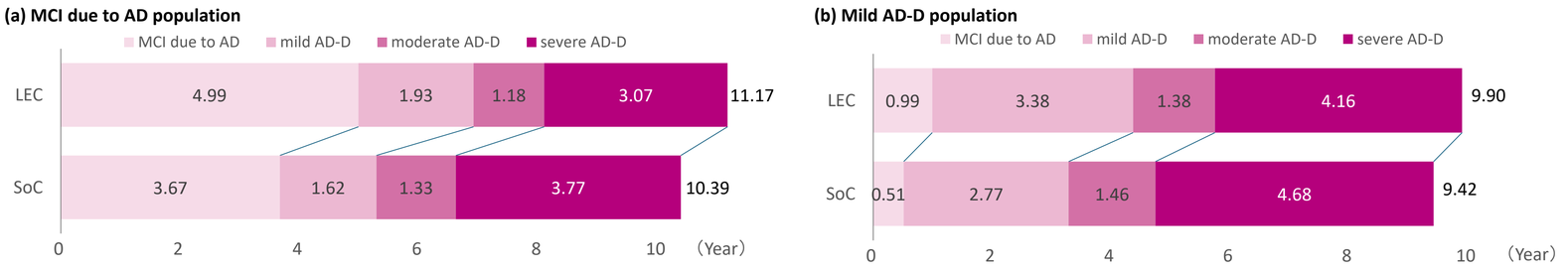


Table 5. Base-case results

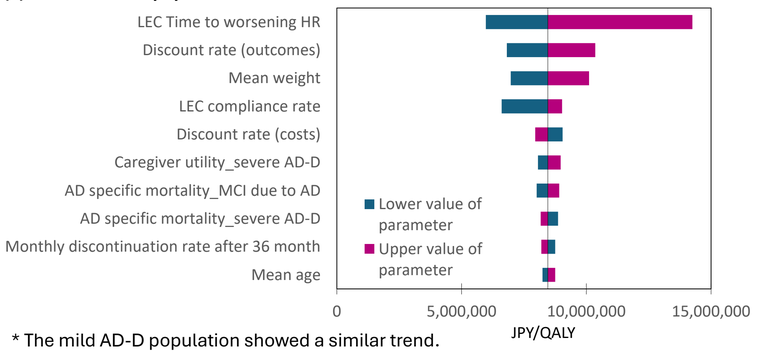
	MCI due to AD population			Mild AD-D population		
	SoC	LEC + SoC	Δ	SoC	LEC + SoC	Δ
Total QALYs (discounted)	14.05	15.36	1.31	12.15	13.00	0.85
Patient QALYs	6.21	6.96	0.75	5.10	5.59	0.49
Caregiver QALYs	7.84	8.40	0.56	7.06	7.42	0.36
Time on treatment (undiscounted, years)	-	4.18	-	-	2.41	-
Total costs (JPY, discounted))	15,386,703	26,462,950	11,076,246	18,904,147	25,556,866	6,652,719
Lecanemab drug cost	0	12,113,548	12,113,548	0	7,157,157	7,157,157
Administration costs	0	187,449	187,449	0	110,752	110,752
Monitoring costs	0	183,795	183,795	0	130,221	130,221
Screening costs	0	117,928	117,928	0	117,928	117,928
Symptomatic treatment costs	52,737	47,086	-5,651	70,666	69,057	-1,610
Direct medical costs	5,466,298	5,114,354	-351,944	6,429,587	6,271,311	-158,276
AE costs	1,485	4,573	3,087	1,485	4,573	3,087
Long-term care costs	9,866,183	8,694,217	-1,171,966	12,402,408	11,695,868	-706,541
ICER (JPY per QALY)	-	-	8,456,482	-	-	7,858,671
VBP: Estimated annual drug cost of lecanemab (JPY)						
WTP threshold of JPY 5 million	-	-	1,863,420	-	-	1,969,370
WTP threshold of JPY 7.5 million	-	-	2,667,730	-	-	2,849,288
WTP threshold of JPY 10 million	-	-	3,472,118	-	-	3,729,128
WTP threshold of JPY 15 million	-	-	5,080,738	-	-	5,488,808

Figure 3. Mean patient life years (undiscounted)



- The most influential parameter was the treatment effect of lecanemab, followed by the discount rate for health outcomes and body weight.(Figure 4)
- When the ICER thresholds of JPY 5 million/QALY and JPY 7.5 million/QALY were applied, the probabilities of lecanemab being cost-effective were 1.2% and 30.8% in the MCI due to AD population, and 4.4% and 42.7% in the mild AD-D population, respectively. (Figure 5)
- The cost-effectiveness improved when the starting age was younger.(Table 6)
- Introducing a maintenance dose every four weeks after 18 months reduced the ICER, bringing it closer to JPY 5 million per QALY.(Table 6)

Figure 4. Deterministic sensitivity analysis results



* The mild AD-D population showed a similar trend.

Figure 5. Cost-effectiveness plane

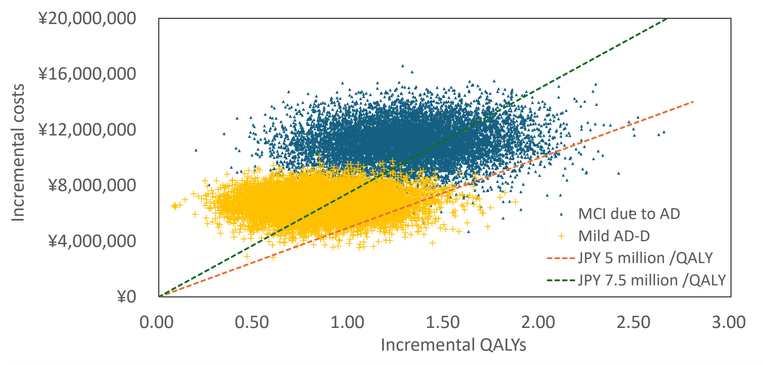


Table 6. Results of scenario analyses

		MCI due to AD population: Treatment	Total costs (JPY)	Total QALYs	ICER (JPY/QALY)	Mild AD population: Total costs (JPY)	Total QALYs	ICER (JPY/QALY)
Scenario analysis: Perspective								
public healthcare payer		LEC	17,768,733	15.36	9,351,254	13,860,998	13.00	8,693,287
		SoC	5,520,520	14.05	-	6,501,738	12.15	-
societal		LEC	40,947,778	15.36	7,676,227	42,823,883	13.00	7,269,665
		SoC	30,893,505	14.05	-	36,669,784	12.15	-
Scenario analysis: Caregiver utility approach								
decrement method		LEC	26,462,950	6.65	13,813,361	25,556,866	5.14	12,754,239
		SoC	15,386,703	5.85	-	18,904,147	4.62	-
increment method		LEC	26,462,950	7.84	12,653,172	25,556,866	6.21	11,712,102
		SoC	15,386,703	6.96	-	18,904,147	5.64	-
Scenario analysis: Relative efficacy for lecanemab								
HR: 0.729		SoC	26,433,779	15.25	9,204,595	25,539,536	12.93	8,505,677
		LEC	15,386,703	14.05	-	18,904,147	12.15	-
HR: 0.679		LEC	26,492,151	15.48	7,796,907	25,574,446	13.07	7,277,191
		SoC	15,386,703	14.05	-	18,904,147	12.15	-
Scenario analysis: Starting age								
65 years		LEC	34,019,045	18.71	7,689,402	34,077,388	16.30	7,371,677
		SoC	23,194,433	17.30	-	27,672,909	15.43	-
75 years		LEC	22,791,592	13.49	9,170,456	21,473,713	11.22	8,365,020
		SoC	11,778,711	12.29	-	14,768,980	10.42	-
Scenario analysis: Maintenance dose								
Administration every 4 weeks after 18 months		LEC	22,429,150	15.36	5,376,761	23,758,703	13.00	5,734,551
		SoC	15,386,703	14.05	-	18,904,147	12.15	-
Scenario analysis: Relative efficacy for lecanemab in moderate AD-D								
Persistence up to moderate AD-D		LEC	41,001,767	15.55	6,771,221	42,853,118	13.23	5,760,140
		SoC	30,893,505	14.06	-	36,669,784	12.16	-

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CONCLUSIONS

- Treatment with lecanemab has been suggested to benefit patients with AD and caregivers, compared with only SoC, by prolonging the duration of early AD and shortening the period of moderate and severe stages, thereby reducing mortality, maintaining health-related quality of life, lowering caregiver burden, and reducing the use of medical and long-term care resources.
- The VBP or the ICER of lecanemab varied greatly depending on the perspectives and the methods of reflecting caregiver QOL. In AD, where the progression of the illness spans a long period and had a significant impact on families and society, narrowly defined value assessments were not sufficient, indicating the need to consider broader social value.