

Predicting the Societal Value of Lecanemab in Early Alzheimer's Disease in Japan: A Patient-Level Simulation

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Table S1. Scenario Analysis Results: WTP Threshold of JPY 10,000,000

	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Base-case analysis	0.73	0.91	-¥1,152,772	¥2,943,264	-	0.73	0.96	-¥1,989,509	¥3,307,279	-
Subsets										
By disease severity and baseline age										
MCI due to AD	0.75	0.95	-¥1,303,188	¥2,868,958	-3%	0.75	1.00	-¥2,268,671	¥3,253,093	-2%
Mild AD dementia	0.68	0.83	-¥637,518	¥3,208,989	9%	0.68	0.85	-¥697,658	¥3,301,141	0%
Mean BL age 65	0.90	1.23	-¥1,976,810	¥3,689,508	25%	0.90	1.30	-¥3,440,445	¥4,246,485	28%
Mean BL age 70	0.78	0.99	-¥1,286,836	¥3,126,633	6%	0.79	1.05	-¥2,182,177	¥3,504,823	6%
Mean BL age 75	0.68	0.83	-¥929,717	¥2,672,828	-9%	0.68	0.87	-¥1,534,841	¥2,950,582	-11%
MCI due to AD + mean BL age 65	0.90	1.27	-¥1,995,240	¥3,541,801	20%	0.90	1.34	-¥3,536,897	¥4,087,499	24%
Symptomatic drug use										
Yes	0.70	0.89	-¥1,043,318	¥2,931,409	0%	0.70	0.91	-¥1,658,206	¥3,226,003	-2%
No	0.77	0.99	-¥1,354,713	¥2,843,680	-3%	0.78	1.04	-¥2,505,201	¥3,267,290	-1%
APOE4										
Carrier	0.70	0.88	-¥1,101,778	¥2,833,280	-4%	0.70	0.92	-¥1,845,541	¥3,162,911	-4%
Non-carrier	0.75	0.95	-¥1,238,459	¥3,016,858	3%	0.75	1.00	-¥2,215,724	¥3,419,346	3%
CSF t-tau level										
1st quintile	0.96	1.22	-¥1,794,416	¥3,437,142	17%	0.95	1.29	-¥3,497,980	¥4,019,354	22%
2nd quintile	0.78	0.97	-¥1,237,666	¥3,012,324	2%	0.78	1.02	-¥2,100,325	¥3,379,163	2%
3rd quintile	0.70	0.87	-¥1,030,485	¥2,814,510	-4%	0.69	0.91	-¥1,799,036	¥3,154,427	-5%
4th quintile	0.64	0.79	-¥838,066	¥2,636,763	-10%	0.64	0.82	-¥1,268,672	¥2,861,499	-13%
5th quintile	0.56	0.69	-¥767,586	¥2,443,305	-17%	0.55	0.72	-¥1,190,584	¥2,668,637	-19%
Time horizon										
5 years	0.03	0.10	-¥520,901	¥497,978	-83%	0.02	0.12	-¥1,238,772	¥824,047	-75%
10 years	0.26	0.48	-¥1,393,138	¥1,812,087	-38%	0.26	0.53	-¥2,687,816	¥2,344,108	-29%
Mortality approach										
Wimo 2020 ³⁰	0.71	0.93	-¥1,373,772	¥3,000,919	2%	0.71	0.98	-¥2,374,004	¥3,423,966	4%
Anderson 2010 ³¹	0.81	0.94	-¥744,222	¥2,941,742	0%	0.82	0.97	-¥1,283,525	¥3,194,173	-3%

	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Takata 2014 ^{29*}	0.67	0.88	-¥1,264,455	¥2,888,475	-2%	0.68	0.93	-¥2,207,191	¥3,294,173	0%
Patient utility										
Neumann 1999	0.73	0.73	-¥1,152,772	¥2,417,653	-18%	0.73	0.77	-¥1,989,509	¥2,781,667	-16%
Landeiro 2020 ⁴⁶	0.73	0.82	-¥1,152,772	¥2,663,708	-9%	0.73	0.86	-¥1,989,509	¥3,027,723	-8%
Institutionalization risk										
Davis 2018 ³⁴	0.73	0.92	-¥1,230,572	¥2,989,591	2%	0.73	0.96	-¥1,846,221	¥3,290,241	-1%
Screening costs										
95% CSF tests and 5% amyloid test	0.73	0.91	-¥1,206,498	¥2,958,662	1%	0.73	0.96	-¥2,043,235	¥3,322,677	0%
Treatment stopping rule										
BC rule + 1.5 DoT	0.43	0.54	-¥676,923	¥1,877,640	-36%	0.42	0.58	-¥1,211,065	¥2,127,775	-36%
BC rule + 3.0 DoT	0.64	0.80	-¥998,809	¥2,623,006	-11%	0.63	0.84	-¥1,723,355	¥2,946,643	-11%
BC rule + 5.0 DoT	0.69	0.86	-¥1,072,805	¥2,797,991	-5%	0.68	0.90	-¥1,833,645	¥3,135,432	-5%
BC rule + 1.5 DoT + maintain reduced amyloid level	0.58	0.72	-¥884,903	¥2,412,396	-18%	0.57	0.76	-¥1,533,316	¥2,708,569	-18%
Treatment dosing										
1.5 years biweekly + Q4W thereafter	0.73	0.91	-¥1,152,772	¥4,168,467	42%	0.73	0.96	-¥1,989,509	¥4,684,012	42%
Alternative discontinuation rates										
0%	0.89	1.11	-¥1,451,133	¥2,447,664	-17%	0.88	1.16	-¥2,516,957	¥2,757,602	-17%
6.9% (over 18 months)	0.82	1.02	-¥1,323,669	¥2,672,727	-9%	0.82	1.08	-¥2,270,736	¥3,002,466	-9%
Cost										
Nakanishi 2021 ⁵⁰	0.73	0.91	-¥221,159	¥2,676,260	-9%	0.73	0.96	-¥673,317	¥2,930,053	-11%

† Percent (%) change in value vs. base case.

‡ This scenario applied updated MMSE thresholds to the HRs from Takata 2014. The updated MMSE thresholds were - 26-29 for MCI due to AD; 21-25 for Mild AD; 11-20 for Moderate AD; 1-10 for Severe AD.

Abbreviations: AD = Alzheimer's disease; APOE4 = apolipoprotein E4; BC = base case, BL = baseline, CSF = cerebrospinal fluid; DoT = duration of treatment in years, LY = life year; MCI = mild cognitive impairment; Q4W = every four weeks; QALY = quality-adjust

Table S2. Scenario Analysis Results: WTP Threshold of JPY 7,500,000

	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Base-case analysis	0.73	0.91	-¥1,152,772	¥2,290,045	-	0.73	0.96	-¥1,989,509	¥2,623,009	-
Subsets										
By disease severity and baseline age										
MCI due to AD	0.75	0.95	-¥1,303,188	¥2,237,878	-2%	0.75	1.00	-¥2,268,671	¥2,589,811	-1%
Mild AD dementia	0.68	0.83	-¥637,518	¥2,463,870	8%	0.68	0.85	-¥697,658	¥2,538,373	-3%
Mean BL age 65	0.90	1.23	-¥1,976,810	¥2,894,636	26%	0.90	1.30	-¥3,440,445	¥3,406,773	30%
Mean BL age 70	0.78	0.99	-¥1,286,836	¥2,434,244	6%	0.79	1.05	-¥2,182,177	¥2,779,996	6%
Mean BL age 75	0.68	0.83	-¥929,717	¥2,071,753	-10%	0.68	0.87	-¥1,534,841	¥2,323,763	-11%
MCI due to AD + mean BL age 65	0.90	1.27	-¥1,995,240	¥2,776,851	21%	0.90	1.34	-¥3,536,897	¥3,279,232	25%
Symptomatic drug use										
Yes	0.70	0.89	-¥1,043,318	¥2,276,211	-1%	0.70	0.91	-¥1,658,206	¥2,542,923	-3%
No	0.77	0.99	-¥1,354,713	¥2,218,736	-3%	0.78	1.04	-¥2,505,201	¥2,609,459	-1%
APOE4										
Carrier	0.70	0.88	-¥1,101,778	¥2,203,396	-4%	0.70	0.92	-¥1,845,541	¥2,503,568	-5%
Non-carrier	0.75	0.95	-¥1,238,459	¥2,349,528	3%	0.75	1.00	-¥2,215,724	¥2,719,954	4%
CSF t-tau level										
1st quintile	0.96	1.22	-¥1,794,416	¥2,687,704	17%	0.95	1.29	-¥3,497,980	¥3,228,649	23%
2nd quintile	0.78	0.97	-¥1,237,666	¥2,344,268	2%	0.78	1.02	-¥2,100,325	¥2,678,660	2%
3rd quintile	0.70	0.87	-¥1,030,485	¥2,185,513	-5%	0.69	0.91	-¥1,799,036	¥2,496,111	-5%
4th quintile	0.64	0.79	-¥838,066	¥2,040,640	-11%	0.64	0.82	-¥1,268,672	¥2,241,597	-15%
5th quintile	0.56	0.69	-¥767,586	¥1,893,623	-17%	0.55	0.72	-¥1,190,584	¥2,096,316	-20%
Time horizon										
5 years	0.03	0.10	-¥520,901	¥416,800	-82%	0.02	0.12	-¥1,238,772	¥721,048	-73%
10 years	0.26	0.48	-¥1,393,138	¥1,461,117	-36%	0.26	0.53	-¥2,687,816	¥1,954,972	-25%
Mortality approach										
Wimo 2020 ³⁰	0.71	0.93	-¥1,373,772	¥2,347,617	3%	0.71	0.98	-¥2,374,004	¥2,735,476	4%
Anderson 2010 ³¹	0.81	0.94	-¥744,222	¥2,260,535	-1%	0.82	0.97	-¥1,283,525	¥2,489,155	-5%

	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Takata 2014 ^{29*}	0.67	0.88	-¥1,264,455	¥2,257,277	-1%	0.68	0.93	-¥2,207,191	¥2,629,338	0%
Patient utility										
Neumann 1999	0.73	0.73	-¥1,152,772	¥1,895,837	-17%	0.73	0.77	-¥1,989,509	¥2,228,801	-15%
Landeiro 2020 ⁴⁶	0.73	0.82	-¥1,152,772	¥2,080,378	-9%	0.73	0.86	-¥1,989,509	¥2,413,342	-8%
Institutionalization risk										
Davis 2018 ³⁴	0.73	0.92	-¥1,230,572	¥2,330,365	2%	0.73	0.96	-¥1,846,221	¥2,599,964	-1%
Screening costs										
95% CSF tests and 5% amyloid test	0.73	0.91	-¥1,206,498	¥2,305,443	1%	0.73	0.96	-¥2,043,235	¥2,638,407	1%
Treatment stopping rule										
BC rule + 1.5 DoT	0.43	0.54	-¥676,923	¥1,459,992	-36%	0.42	0.58	-¥1,211,065	¥1,688,437	-36%
BC rule + 3.0 DoT	0.64	0.80	-¥998,809	¥2,040,022	-11%	0.63	0.84	-¥1,723,355	¥2,335,535	-11%
BC rule + 5.0 DoT	0.69	0.86	-¥1,072,805	¥2,176,076	-5%	0.68	0.90	-¥1,833,645	¥2,484,179	-5%
BC rule + 1.5 DoT + maintain reduced amyloid level	0.58	0.72	-¥884,903	¥1,875,286	-18%	0.57	0.76	-¥1,533,316	¥2,145,770	-18%
Treatment dosing										
1.5 years biweekly + Q4W thereafter	0.73	0.91	-¥1,152,772	¥3,243,331	42%	0.73	0.96	-¥1,989,509	¥3,714,899	42%
Alternative discontinuation rates										
0%	0.89	1.11	-¥1,451,133	¥1,906,531	-17%	0.88	1.16	-¥2,516,957	¥2,190,973	-16%
6.9% (over 18 months)	0.82	1.02	-¥1,323,669	¥2,080,911	-9%	0.82	1.08	-¥2,270,736	¥2,382,853	-9%
Cost										
Nakanishi 2021 ⁵⁰	0.73	0.91	-¥221,159	¥2,023,041	-12%	0.73	0.96	-¥673,317	¥2,245,784	-14%

† Percent (%) change in value vs. base case.

‡ This scenario applied updated MMSE thresholds to the HRs from Takata 2014. The updated MMSE thresholds were - 26-29 for MCI due to AD; 21-25 for Mild AD; 11-20 for Moderate AD; 1-10 for Severe AD.

Abbreviations: AD = Alzheimer's disease; APOE4 = apolipoprotein E4; BC = base case, BL = baseline, CSF = cerebrospinal fluid; DoT = duration of treatment in years, LY = life year; MCI = mild cognitive impairment; Q4W = every four weeks; QALY = quality-adjust

Table S3. Scenario Analysis Results: WTP Threshold of JPY 5,000,000

	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Base-case analysis	0.73	0.91	-¥1,152,772	¥1,636,827	-	0.73	0.96	-¥1,989,509	¥1,938,740	-
Subsets										
By disease severity and baseline age										
MCI due to AD	0.75	0.95	-¥1,303,188	¥1,606,797	-2%	0.75	1.00	-¥2,268,671	¥1,926,529	-1%
Mild AD dementia	0.68	0.83	-¥637,518	¥1,718,751	5%	0.68	0.85	-¥697,658	¥1,775,606	-8%
Mean BL age 65	0.90	1.23	-¥1,976,810	¥2,099,763	28%	0.90	1.30	-¥3,440,445	¥2,567,061	32%
Mean BL age 70	0.78	0.99	-¥1,286,836	¥1,741,854	6%	0.79	1.05	-¥2,182,177	¥2,055,170	6%
Mean BL age 75	0.68	0.83	-¥929,717	¥1,470,679	-10%	0.68	0.87	-¥1,534,841	¥1,696,944	-12%
MCI due to AD + mean BL age 65	0.90	1.27	-¥1,995,240	¥2,011,902	23%	0.90	1.34	-¥3,536,897	¥2,470,964	27%
Symptomatic drug use										
Yes	0.70	0.89	-¥1,043,318	¥1,621,013	-1%	0.70	0.91	-¥1,658,206	¥1,859,842	-4%
No	0.77	0.99	-¥1,354,713	¥1,593,793	-3%	0.78	1.04	-¥2,505,201	¥1,951,628	1%
APOE4										
Carrier	0.70	0.88	-¥1,101,778	¥1,573,512	-4%	0.70	0.92	-¥1,845,541	¥1,844,225	-5%
Non-carrier	0.75	0.95	-¥1,238,459	¥1,682,197	3%	0.75	1.00	-¥2,215,724	¥2,020,561	4%
CSF t-tau level										
1st quintile	0.96	1.22	-¥1,794,416	¥1,938,267	18%	0.95	1.29	-¥3,497,980	¥2,437,945	26%
2nd quintile	0.78	0.97	-¥1,237,666	¥1,676,212	2%	0.78	1.02	-¥2,100,325	¥1,978,158	2%
3rd quintile	0.70	0.87	-¥1,030,485	¥1,556,516	-5%	0.69	0.91	-¥1,799,036	¥1,837,795	-5%
4th quintile	0.64	0.79	-¥838,066	¥1,444,518	-12%	0.64	0.82	-¥1,268,672	¥1,621,696	-16%
5th quintile	0.56	0.69	-¥767,586	¥1,343,941	-18%	0.55	0.72	-¥1,190,584	¥1,523,996	-21%
Time horizon										
5 years	0.03	0.10	-¥520,901	¥335,622	-79%	0.02	0.12	-¥1,238,772	¥618,049	-68%
10 years	0.26	0.48	-¥1,393,138	¥1,110,147	-32%	0.26	0.53	-¥2,687,816	¥1,565,835	-19%
Mortality approach										
Wimo 2020 ³⁰	0.71	0.93	-¥1,373,772	¥1,694,316	4%	0.71	0.98	-¥2,374,004	¥2,046,985	6%
Anderson 2010 ³¹	0.81	0.94	-¥744,222	¥1,579,328	-4%	0.82	0.97	-¥1,283,525	¥1,784,137	-8%

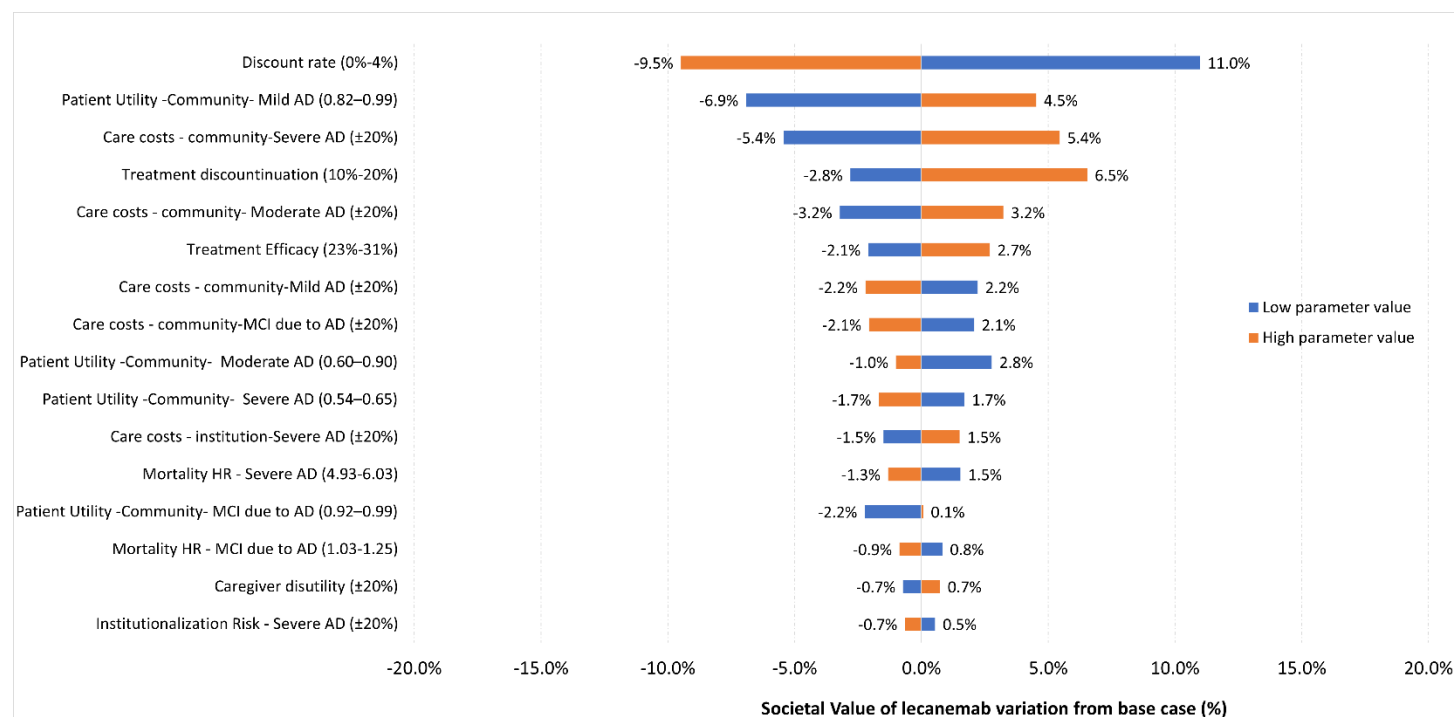
	Healthcare Payer's Perspective					Societal Perspective				
	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†	Δ LYs	Δ QALYs	Δ costs	Value	% Δ†
Takata 2014 ^{29*}	0.67	0.88	-¥1,264,455	¥1,626,079	-1%	0.68	0.93	-¥2,207,191	¥1,964,503	1%
Patient utility										
Neumann 1999	0.73	0.73	-¥1,152,772	¥1,374,021	-16%	0.73	0.77	-¥1,989,509	¥1,675,934	-14%
Landeiro 2020 ⁴⁶	0.73	0.82	-¥1,152,772	¥1,497,048	-9%	0.73	0.86	-¥1,989,509	¥1,798,962	-7%
Institutionalization risk										
Davis 2018 ³⁴	0.73	0.92	-¥1,230,572	¥1,671,139	2%	0.73	0.96	-¥1,846,221	¥1,909,687	-1%
Screening costs										
95% CSF tests and 5% amyloid test	0.73	0.91	-¥1,206,498	¥1,652,224	1%	0.73	0.96	-¥2,043,235	¥1,954,138	1%
Treatment stopping rule										
BC rule + 1.5 DoT	0.43	0.54	-¥676,923	¥1,042,344	-36%	0.42	0.58	-¥1,211,065	¥1,249,099	-36%
BC rule + 3.0 DoT	0.64	0.80	-¥998,809	¥1,457,038	-11%	0.63	0.84	-¥1,723,355	¥1,724,428	-11%
BC rule + 5.0 DoT	0.69	0.86	-¥1,072,805	¥1,554,162	-5%	0.68	0.90	-¥1,833,645	¥1,832,927	-5%
BC rule + 1.5 DoT + maintain reduced amyloid level	0.58	0.72	-¥884,903	¥1,338,177	-18%	0.57	0.76	-¥1,533,316	¥1,582,971	-18%
Treatment dosing										
1.5 years biweekly + Q4W thereafter	0.73	0.91	-¥1,152,772	¥2,318,194	42%	0.73	0.96	-¥1,989,509	¥2,745,786	42%
Alternative discontinuation rates										
0%	0.89	1.11	-¥1,451,133	¥1,365,399	-17%	0.88	1.16	-¥2,516,957	¥1,624,345	-16%
6.9% (over 18 months)	0.82	1.02	-¥1,323,669	¥1,489,094	-9%	0.82	1.08	-¥2,270,736	¥1,763,241	-9%
Cost										
Nakanishi 2021 ⁵⁰	0.73	0.91	-¥221,159	¥1,369,823	-16%	0.73	0.96	-¥673,317	¥1,561,514	-19%

† Percent (%) change in value vs. base case.

‡ This scenario applied updated MMSE thresholds to the HRs from Takata 2014. The updated MMSE thresholds were - 26-29 for MCI due to AD; 21-25 for Mild AD; 11-20 for Moderate AD; 1-10 for Severe AD.

Abbreviations: AD = Alzheimer's disease; APOE4 = apolipoprotein E4; BC = base case, BL = baseline, CSF = cerebrospinal fluid; DoT = duration of treatment in years, LY = life year; MCI = mild cognitive impairment; Q4W = every four weeks; QALY = quality-adjust

Figure S1. One-way Sensitivity Analyses Results – WTP threshold of ¥5,000,000



AD = Alzheimer's disease, CDR-SB = Clinical Dementia Rating Sum of Boxes, HR = hazard ratio; MCI = mild cognitive impairment; Societal Value of lecanemab = ¥5,000,000