Long-Term Health Outcomes of Lecanemab in Patients with Early Alzheimer's Disease Using Simulation Modeling

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SUPPLEMENTARY MATERIAL

Supplementary Table S1. Patient Characteristics for Subsets Explored in Scenario Analyses

Baseline Characteristic	MCI Due to AD	Mild AD Dementia	Mean Baseline Age of 65 years	MCI due to AD and mean baseline age of 65 years	CSF t-tau Quintile				
					1st	2nd	3rd	4th	5th
Number of ADNI patients in the subset	352	77	149	123	85	87	85	87	85
Age, median (range), years	72 (55-80)	73 (55-80)	65 (55-70)	65 (55-70)	71 (55-80)	71 (55-80)	71 (55-80)	72 (55-80)	72 (55-80)
PET SUVr, mean (SD)	1.37 (0.14)	1.40 (0.15)	1.36 (0.14)	1.35 (0.14)	1.33 (0.14)	1.40 (0.14)	1.36 (0.13)	1.38 (0.14)	1.40 (0.15)
MMSE, mean (SD)	26.34 (2.03)	24.16 (1.50)	26.17 (2.08)	26.61 (1.92)	26.68 (2.14)	26.02 (2.1)	25.91 (2.27)	25.76 (2.07)	25.35 (1.86)
CDR-SB, mean (SD)	2.21 (0.93)	5.33 (1.04)	2.64 (1.48)	2.13 (0.92	2.45 (1.41)	2.76 (1.64)	2.78 (1.45)	2.77 (1.55)	3.01 (1.51)

Abbreviations: AD = Alzheimer's disease; ADNI = Alzheimer's Disease Neuroimaging Initiative; CDR-SB = Clinical Dementia Rating Sum of Boxes; CSF t-tau = cerebrospinal fluid total-tau; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; PET = positron emission tomography; SUVr = standard uptake value ratio

Supplementary Table S2. Base-case Model Outcomes over 5- and 10-Year Time horizons

Modeled Health Outcomes	5-year Time Horizon			10-year Time Horizon		
	SoC	Lecanemab + SoC	Incremental	SoC	Lecanemab + SoC	Incremental
Patients with/progressed to mild AD dementia, %	**83%**	**69%**	**-14%**	**90%**	**81%**	**-9%**
Patients with mild AD dementia at baseline	17%	17%	0%	17%	17%	0%
Patients progressed to mild AD dementia	66%	52%	-14%	73%	64%	-9%
Patients progressed to moderate AD dementia, %	**33%**	**18%**	**-15%**	**58%**	**42%**	**-16%**
Patients progressed to severe AD dementia, %	**3%**	**1%**	**-2%**	**29%**	**17%**	**-12%**
Patients institutionalized, %	**9%**	**7%**	**-2%**	**26%**	**19%**	**-7%**
Patients discontinued treatment, %	**NA**	**18%**	**NA**	**NA**	**40%**	**NA**
Mean time to event[†] (undiscounted, years)						
Mild AD	2.49 (2.39 - 2.58)	3.19 (3.09 - 3.28)	0.7	2.83 (2.68 - 2.99)	4.23 (4.03 - 4.43)	1.4
Moderate AD	4.24 (4.17 - 4.30)	4.52 (4.45 - 4.58)	0.28	5.50 (5.33 - 5.68)	6.77 (6.58 - 6.96)	1.27
Severe AD	4.87 (4.83 - 4.89)	4.90 (4.85 - 4.92)	0.03	7.73 (7.56 - 7.89)	8.42 (8.25 - 8.58)	0.69
Institutional care	3.09 (2.82 - 3.32)	3.02 (2.70 - 3.29)	-0.07	5.79 (5.48 - 6.07)	5.84 (5.47 - 6.18)	0.05

Median time to event (years)						
Mild AD	2.15	3.14	0.99	2.15	3.14	0.99
Moderate AD	NR	NR	NA	5.10	6.75	1.65
Severe AD	NR	NR	NA	7.77	8.89	1.13
Institutional care	3.26	3.16	-0.10	6.06	6.05	-0.01
Median time to event (of those alive) (years)						
Mild AD	1.84	2.71	0.87	1.84	2.71	0.87
Moderate AD	NR	NR	NA	5.59	9.03	3.44
Severe AD	NR	NR	NA	NR	NR	NA
Institutional care	NR	NR	NA	NR	NR	NA
Time on treatment (undiscounted, years)						
Total LYs (undiscounted)	**4.27 (4.22 - 4.33)**	**4.33 (4.28 - 4.39)**	**0.06**	**6.54 (6.41 - 6.67)**	**6.93 (6.80 - 7.06)**	**0.39**
Time in community care	**4.12**	**4.21**	**0.09**	**5.89**	**6.42**	**0.53**
MCI due to AD	2.11	2.61	0.5	2.36	3.31	0.95
Mild AD	1.72	1.46	-0.26	2.34	2.32	-0.02
Moderate AD	0.28	0.15	-0.13	0.97	0.68	-0.29
Severe AD	0.01	0	-0.01	0.22	0.11	-0.11
Time in institutional care	**0.15 (0.12 - 0.18)**	**0.12 (0.10 - 0.14)**	**-0.03**	**0.65 (0.59 - 0.72)**	**0.51 (0.45 - 0.57)**	**-0.14**
MCI due to AD	0	0	0	0.00	0.00	0.00
Mild AD	0.08	0.09	0	0.13	0.16	0.03
Moderate AD	0.06	0.03	-0.03	0.29	0.22	-0.07
Severe AD	0	0	0	0.23	0.13	-0.11
Total LYs (discounted)	**3.99**	**4.04**	**0.05**	**5.82**	**6.14**	**0.31**
Total QALYs (discounted)	**2.94 (2.90 - 2.98)**	**3.05 (3.01 - 3.09)**	**0.11**	**3.97 (3.89 - 4.04)**	**4.40 (4.32 - 4.48)**	**0.43**
Patient QALYs, total	3.02	3.11	0.09	3.80	4.26	0.46
Lost to ARIA AEs	NA	0.001	NA	NA	-0.001	NA
Caregiver QALYs lost	0.077	0.058	-0.02	-0.17	-0.14	0.03
Total EvLYG (discounted)	**2.94**	**3.06**	**0.12**	**3.97**	**4.46**	**0.49**

Abbreviations: AD = Alzheimer's disease; AE = adverse event; ARIA = amyloid-related imaging abnormalities; EvLYG = equal value of life-years gained; LY = life-year; MCI = mild cognitive impairment; NA = not applicable; QALY = quality-adjusted life-year; SoC = standard of care

[†]The average survival from time 0 to a specified time point was estimated as the area under the survival curve up to that point.

Supplementary Table S3. Scenario Analysis Results (Median Time to Event)

Scenarios	Median Time to Mild AD Dementia			Median Time to Moderate AD Dementia		
	SoC	Lecanemab + SoC	INC	SoC	Lecanemab + SoC	INC
Base-case analysis	2.15	3.14	0.99	5.15	7.10	1.95
Subsets (base-case population: MCI due to AD and mild AD dementia with confirmed Aβ pathology)						
Disease severity and baseline age						
MCI due to AD	2.14	3.32	1.18	5.64	7.81	2.17
Mild AD dementia	NA	NA	NA	2.93	3.81	0.89
Mean baseline age of 65 years	2.43	3.83	1.40	5.43	7.40	1.97
MCI due to AD + mean baseline age of 65 years	2.54	3.99	1.45	6.03	8.32	2.29
CSF t-tau level						
1st CSF t-tau quintile	2.77	4.90	2.13	6.50	9.20	2.70
2nd CSF t-tau quintile	2.25	3.62	1.37	5.44	7.53	2.10
3rd CSF t-tau quintile	2.25	3.48	1.23	5.35	7.53	2.18
4th CSF t-tau quintile	2.01	2.91	0.91	5.05	6.93	1.87
5th CSF t-tau quintile	1.81	2.36	0.56	4.33	5.62	1.30
Time horizon (base-case: lifetime)						
5 years	-	-	-	NR	NR	NA
10 years	-	-	-	5.10	6.75	1.65
Mortality approach (base-case source: Andersen et al. 2010)						
Wimo et al. 2020	2.16	3.14	0.99	4.94	6.56	1.63
Annual discontinuation risk (base-case: 0.0%)						
10.00%	-	3.13	0.97	-	7.07	1.92
17.3% (risk observed in trial)	-	3.11	0.96	-	6.91	1.76
20.00%	-	3.10	0.94	-	6.90	1.75
Treatment stopping rule (base-case rule: stop at moderate AD dementia)						
Base-case rule + 1.5 years treatment duration	-	3.08	0.92	-	6.48	1.33
Base-case rule + 1.5 years treatment duration + maintain reduced amyloid level	-	3.04	0.89	-	6.76	1.61
Base-case rule + 3 years treatment duration	-	3.14	0.99	-	7.18	2.03
Base-case rule + 5 years treatment duration	-	3.14	0.99	-	7.21	2.06

Abbreviations: Aβ beta-amyloid; AD = Alzheimer's disease; CSF t-tau = cerebrospinal fluid total-tau; INC = incremental; MCI = Mild cognitive impairment; SoC= standard of care

Supplementary Table S4. Scenario Analysis Results (Median Time to Event [of Those Alive])

Scenarios	Median Time to Mild AD Dementia			Median Time to Moderate AD Dementia		
	SoC	Lecanemab + SoC	INC	SoC	Lecanemab + SoC	INC
Base-case analysis	1.84	2.71	0.87	5.59	9.03	3.44
Subsets (base-case population: MCI due to AD and mild AD dementia with confirmed Aβ pathology)						
Disease severity and baseline age						
MCI due to AD	2.23	3.55	1.32	6.01	9.79	3.78
Mild AD dementia	NA	NA	NA	2.90	3.83	0.93
Mean baseline age of 65 years	2.08	3.15	1.07	5.88	9.10	3.22
MCI due to AD + mean baseline age of 65 years	2.57	4.15	1.58	6.51	11.23	4.71
CSF t-tau level						
1st CSF t-tau quintile	2.61	4.84	2.23	7.61	NR	NA
2nd CSF t-tau quintile	1.91	2.97	1.06	5.85	NR	NA
3rd CSF t-tau quintile	1.85	2.74	0.89	5.74	8.95	3.21
4th CSF t-tau quintile	1.75	2.48	0.74	5.34	7.83	2.48
5th CSF t-tau quintile	1.46	1.92	0.46	4.58	6.04	1.46
Time horizon (base-case: lifetime)						
5 years	-	-	-	NR	NR	NA
10 years	-	-	-	5.59	9.03	3.44
Mortality approach (base-case source: Andersen et al. 2010)						
Wimo et al. 2020	1.80	2.54	0.74	5.30	7.51	2.21
Annual discontinuation risk (base-case: 0.0%)						
10.00%	-	2.71	0.87	-	8.57	2.99
17.3% (risk observed in trial)	-	2.70	0.86	-	8.39	2.81
20.00%	-	2.70	0.86	-	8.25	2.67
Treatment stopping rule (base-case rule: stop at moderate AD dementia)						
Base-case rule + 1.5 years treatment duration	-	2.72	0.88	-	7.15	1.57
Base-case rule + 1.5 years treatment duration + maintain reduced amyloid level	-	2.67	0.83	-	7.75	2.16
Base-case rule + 3 years treatment duration	-	2.71	0.87	-	8.53	2.95
Base-case rule + 5 years treatment duration	-	2.71	0.87	-	8.86	3.27

Abbreviations: Aβ beta-amyloid; AD = Alzheimer's disease; CSF t-tau = cerebrospinal fluid total-tau; INC = incremental; MCI = Mild cognitive impairment; SoC= standard of care