SUPPLEMENTARY MATERIAL

Estimating the economically justifiable price in the US of limited-duration treatment with donanemab for early symptomatic Alzheimer's disease

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TRAILBLAZER-ALZ 2 Trial Population

Characteristic	Donanemab (n=860)	Placebo (n=876)
Sex, n (%)		
Female	493 (57.3)	503 (57.4)
Male	367 (42.7)	373 (42.6)
Age, mean (SD)	73.0 (6.2)	73.0 (6.2)
Race, n (%)		
American Indian or Alaska Native	2 (0.2)	0 (0.0)
Asian	57 (6.6)	47 (5.4)
Black or African American	19 (2.2)	21 (2.4)
White	781 (90.9)	807 (92.1)
Multiple	0	1 (0.1)
Missing	1 (0.1)	0
APOE genotype, n (%)*		
E2/E2	0	1 (0.1)
E2/E3	18 (2.1)	20 (2.3)
E2/E4	22 (2.6)	25 (2.9)
E3/E3	241 (28.1)	230 (26.4)
E3/E4	433 (50.5)	450 (51.6)
E4/E4	143 (16.7)	146 (16.7)
Amyloid plaque level, mean (SD), Centiloids	103.5 (34.5)	101.6 (34.5)
Neocortical flortaucipir SUVR, mean (SD)	1.34 (0.25)	1.35 (0.26)
Plasma P-tau217, mean (SD), pg/mL	7.5 (18.5)	6.8 (15.4)

*Available for 598 patients in the donanemab arm and 621 in the placebo arm.
APOE = apolipoprotein E; P-tau217 = phosphorylated tau 217; SD = standard deviation; SUVR = standardized uptake value ratio
Source: Sims et al. (1)

Scenario Analysis Detailed Results

Scenario 1: Test for amyloid clearance (treatment completion) only at 6 months; treatment through 18 months

Patients completing treatment based on amyloid plaque clearance at 6 months was set to 29.7%. Remaining patients did not receive an amyloid PET scan at 12 months and did not discontinue donanemab at that time. Instead, they continued donanemab treatment for a maximum of 18 months if they did not progress to severe dementia due to AD. The donanemab one-year (13-dose) EJP at the $150,000 per QALY gained WTP threshold was lowered to $75,400 from the co-base case health care perspective value of $80,538. Compared to the co-base case health care perspective, the reduction in patient direct medical costs by virtue of obtaining only a single amyloid PET scan at 6 months was more than offset by an increase in the average number of donanemab Q4W doses (13.88 vs 12.56). LYs and QALYs are not impacted as the assumed benefit of donanemab treatment is not impacted by treatment duration.

Scenario 2: Test for amyloid clearance (treatment completion) only at 12 months; treatment through 18 months

Patients did not receive amyloid PET scans at 6 months and did not complete donanemab treatment based on amyloid plaque clearance at that time. Patients completing treatment based on amyloid plaque clearance at 12 months was set to 66.1%. Remaining patients continued donanemab treatment for a maximum of 18 months if they did not progress to severe dementia due to AD. The donanemab one-year (13-dose) EJP at the $150,000 per QALY gained WTP threshold was lowered to $77,450 from the co-base case health care perspective value of $80,538. The same rationale as above for Scenario 1 applies for the decrease in the EJP.

Scenario 3: Test for amyloid clearance (treatment completion) only at 12 months; treatment continued through 24 months

Patients did not receive amyloid PET scans at 6 months or complete donanemab treatment based on amyloid plaque clearance at that time. Patients completing treatment based on amyloid plaque clearance at 12 months was set to 66.1%. Remaining patients continued donanemab treatment for a maximum of 24 months if they did not progress to severe dementia due to AD. The donanemab one-year (13-dose) EJP at the $150,000 per QALY gained WTP threshold was lowered to $69,145 from the co-base case health care perspective value of $80,538 The decrease in the EJP compared to the co-base case health care sector perspective was driven by the longer treatment duration, which increased number of donanemab Q4W doses, despite a reduction in direct medical costs by virtue of obtaining only a single amyloid PET scan at 12 months.

Scenario 4: Treatment limited to patients with MCI due to AD

The starting patient population was composed of 100% MCI due to AD patients. The donanemab one-year (13-dose) EJP at the $150,000 per QALY gained WTP threshold was increased to $93,038 from the co-base case health care perspective value of $80,538. Initiating treatment earlier (i.e., exclusively at the MCI due to AD stage) compared to the base case resulted in more LYs and QALYs gained. The relatively small increases in average donanemab doses and resulting acquisition costs and incremental non-treatment costs are offset by the increased QALY gains, resulting in the higher EJP at the specified threshold compared to the co-base case.

Scenario 5: Treatment limited to patients with mild dementia due to AD

The starting patient population was composed of 100% mild dementia due to AD patients. The donanemab one-year (13-dose) EJP at the $150,000 per QALY gained

WTP threshold was lowered to $64,972 from the co-base case health care perspective value of $80,538. Initiating treatment later (i.e., exclusively at the mild dementia due to AD stage) compared to the base case resulted in fewer LYs and QALYs gained. The relatively small decreases in average number of donanemab Q4W doses and resulting acquisition costs and incremental non-treatment costs are offset by the decreased QALY gains, resulting in the higher EJP at the specified threshold compared to the co-base case.

Table 1. Scenario analyses results

	Scenario 1		Scenario 2		Scenario 3		Scenario 4		Scenario 5	
	Incremental Donanemab vs BSC	**Total BSC**	**Incremental Donanemab vs BSC**	**Total BSC**	**Incremental Donanemab vs BSC**	**Total BSC**	**Incremental Donanemab vs BSC**	**Total BSC**	**Incremental Donanemab vs BSC**	**Total BSC**
Costs ($)										
Total non-treatment costs	23,217	214,419	22,514	214,419	22,658	214,419	27,374	215,624	23,743	212,946
Administration costs	885	—	869	—	972	—	813	—	789	—
Long-term care costs	9,608	132,929	9,608	132,929	9,608	132,929	11,723	131,878	7,023	134,213
Patient direct medical costs	12,724	81,490	12,037	81,490	12,079	81,490	14,838	83,746	15,931	78,733
Outcomes										
Avg. # of donanemab Q4W doses[b]	13.88	—	13.61	—	15.27	—	12.73	—	12.35	—
Patient Life Years	0.743	5.584	0.743	5.584	0.743	5.584	0.846	6.229	0.616	4.795
Patient QALYs	0.683	3.329	0.683	3.329	0.683	3.329	0.782	3.964	0.563	2.553
Mean Time in AD State (Years)										
MCI due to AD	0.836	1.980	0.836	1.980	0.836	1.980	1.375	3.445	0.178	0.189
Mild AD	0.560	1.750	0.560	1.750	0.560	1.750	0.295	1.560	0.883	1.982
Moderate AD	0.100	1.104	0.100	1.104	0.100	1.104	−0.032	0.954	0.261	1.288
Severe AD	−0.511	1.442	−0.511	1.442	−0.511	1.442	−0.487	1.118	−0.539	1.839
Time in Long Term Care (Years)	0.169	1.693	0.169	1.693	0.169	1.693	0.206	1.705	0.124	1.678
EJP at $150,000 per QALY										

For 13 q4w doses $	75,400	77,450	69,145	93,038	64,792
Per q4w dose $	5,800	5,958	5,319	7,157	4,984
Per average patient $	80,520	81,064	81,220	91,122	61,551
EJP at $100,000 per QALY					
For 13 q4w doses $	42,908	44,367	39,557	52,581	34,752
Per q4w dose $	3,301	3,413	3,043	4,045	2,673
Per average patient $	45,821	46,438	46,464	51,498	33,014

Scenarios analyses are conducted from the health care system perspective:

- Scenario 1: Test for amyloid clearance (treatment completion) only at 6 months; treatment through 18 months
- Scenario 2: Test for amyloid clearance (treatment completion) only at 12 months; treatment through 18 months
- Scenario 3: Test for amyloid clearance (treatment completion) only at 12 months; treatment continued through 24 months
- Scenario 4: Treatment limited to patients with MCI due to AD
- Scenario 5: Treatment limited to patients with mild dementia due to AD

AD = Alzheimer's disease; BSC = best supportive care; EJP = economically justifiable price; LTC = long-term care; LY = life-year; MCI = mild cognitive impairment; mild AD = mild dementia due to AD, moderate AD = moderate dementia due to AD, severe AD -= severe dementia due to AD; Q4W = every 4 weeks; QALY = quality-adjusted life-year; Tx = treatment; WTP = willingness-to-pay.

References

1. Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, Sparks J, et al. Donanemab in Early Symptomatic Alzheimer's Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. 2023;330(6):512-27.