

Shigeki Hirano¹, Yoshikazu Nakano¹, Mitsuyoshi Tamura¹, Kenta Osawa¹, Yume Koizumi¹, Yutaro Suzuki¹, Kosuke Yamagishi¹, Yoshikazu Chishiki¹, Shogo Furukawa^{1,2}, Ai Ishikawa^{1,3}, Kazuho Kojima⁴, Masahide Suzuki⁵, Setsu Sawai⁶, Masahiro Mori¹

(1) Department of Neurology, Graduate School of Medicine, Chiba University, Chiba, Japan, (2) Department of Neurology, Japanese Red Cross Narita Hospital, Chiba, Japan
(3) Department of Neurology, NHO Chibahigashi National Hospital, Chiba, Japan, (4) Department of Neurology, Chiba Rosai Hospital, Chiba, Japan,
(5) Asahi Neurology Rehabilitation Hospital, Chiba, Japan, (6) Department of Neurology, Aoba Chiba Municipal Hospital, Chiba, Japan

Background/Objectives

The amyloid β (A β) antibody therapy, lecanemab and donanemab against early Alzheimer's disease (AD) were covered by insurance since September 2023 and September 2024, respectively, in Japan. Lecanemab which targets protofibrils is applicable to those with mini-mental state examination (MMSE) 22 – 30, administered every 2 weeks, each drip >60 mins, capable to extend beyond 18 months when needed. Donanemab which targets N3 pyroglutamate-modified amyloid is applicable to those with MMSE 20 – 28, administered every 4 weeks, drip >30 mins, able to re-evaluate A β load by positron emission tomography (PET) at 12 and 18 months, able to complete administration if amyloid PET results were visually negative, administered up to 18 months.

Objective of this study was to compare the difference of baseline demography and efficacy at 6 months between patients receiving lecanemab and donanemab in mild cognitive impairment (MCI) due to AD and mild AD in 5 hospitals located in Chiba, Japan.

Methods

Baseline clinical data comprised of age, sex, duration, clinical dementia rating (CDR), MMSE, centiloid scale of amyloid (¹⁸F-flutemetamol) positron emission tomography (PET), and cerebrospinal fluid (CSF) biomarkers in five hospitals located in Chiba prefecture.

Written informed consent was obtained from all participants.

Baseline demography and 6 months follow up neuropsychological test data were collected. Baseline demography and longitudinal CDR-sum of boxes (SoB) and MMSE change were compared between two treatment groups.

Results (1)

Table 1. Baseline clinical demography of patients with early Alzheimer's disease treated with amyloid antibody therapy

	Lecanemab N=36	Donanemab N=30	P-value
Age	73.0 (6.3)	71.6 (7.2)	0.41
Sex	15M:21F	12M:18F	0.89
Type	29 MCI, 7 AD	18 MCI, 12 AD	N.A.
MMSE	25.3 (2.6)	24.6 (1.98)	0.23
ApoE	Non N=11, homo N=3, homo N=1	Non-carrier 5Hetero N=9 Homo N=1,	N.A.
Duration (y)	1.94 (1.21)	2.30 (1.70)	0.34
Centiloid	62.8 (32.4) [N=19]	72.9 (27.3) [N=22]	0.29
CSF A $\beta_{42/40}$	0.045 (0.012) [N=21]	0.046 (0.010) [N=17]	0.89
CSF P-tau	104.6 (108.6) [N=8]	126 (48.9) [N=10]	0.58
CSF T-tau	651 (560) [N=8]	875 (288) [N=9]	0.30
Dose (mg)	528.1 (101.4)	[Initial] 700mg: 22, 350mg: 8	N.A.
CDR global	0.5: N=31, 1.0: N=5	0.5: N=25, 1.0: N=5	N.A.
CDR SoB	2.56 (1.65)	3.02 (1.32)	0.22

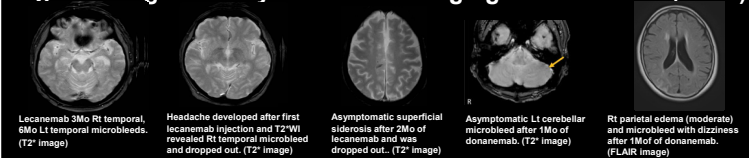
(mean $\pm$ SD)

Table 2. Six months clinical demography of patients with early Alzheimer's disease treated with amyloid antibody therapy

	Lecanemab N=20	Donanemab N=11	P-value
Age	73.6 (5.1)	69.2 (8.9)	0.29
Sex	7M:13F	7M:4F	0.13
Type	16 MCI, 4 AD	6 MCI, 5 AD	N.A.
ApoE	Non N=6, hetero N=3	Non: 3, hetero: 2, homo 1	N.A.
Duration (y)	1.80 (1.35)	3.14 (2.07)	0.26
Centiloid	67.6 (31.3) [N=11]	68.2 (17.2) [N=8]	0.62
CDR global	0.5 N=19, 1.0 N=1	0.5 N=9, 1.0 N=2	N.A.
CDR SoB	2.28 (1.52)	3.0 (1.47)	0.08
Δ CDR-SoB	+0.025 (0.900)	-0.64 (1.07)	0.08
MMSE	25.9 (2.75)	25.1 (2.5)	0.08
Δ MMSE	+0.05 (1.93)	+0.45 (1.37)	0.54
ARIA	ARIA-H 3, ARIA-E 0	ARIA-H 1, ARIA-E 1	N.A.

MMSE: mini-mental stage examination, CSF: cerebrospinal fluid, CDR: clinical dementia rating, SoB: sum of boxes, ARIA: Amyloid related imaging abnormalities, N.A.: Not applicable (mean $\pm$ SD)

Figure. Images of amyloid related imaging abnormalities (ARIA)



Results (2)

- Sixty-six patients (47 MCI, 19 AD) were enrolled (36 lecanemab, 30 donanemab) in this study. All baseline clinical demography did not differ between two treatment groups (Table 1).
- The cognitive tests did not change after 6 months and those changes (Δ CDR sum of boxes, Δ MMSE) did not differ between 20 lecanemab and 11 donanemab groups.
- There were 2 microbleed, 1 superficial siderosis (ARIA: 3/36 8.3%), 1 infusion-related reaction in lecanemab group, 1 microbleed, 1 moderate brain edema (ARIA: 2/30 6.7%), 2 infusion-related reactions in donanemab group.
- In lecanemab group, 2 dropped out because of unwilling to treat, 1 dropped out because of superficial siderosis.
- In donanemab group, 2 dropped out by infusion reaction but those having ARIA continued the injection.

Discussions/Conclusions

In the real world, 6 months observation revealed that cognitive status does not change statistically and does not differ between two treatment groups. No difference were found between lecanemab and donanemab treatment in baseline demography and cognitive changes after 6 months of treatment.

Majorities of adverse events develop within 6 months of treatment. Incidence of ARIA was less than 10%, most of which was asymptomatic microbleeds. Major reason for treatment discontinuation was infusion-related reactions.

[Reference]

- [1] van Dyck CH, Swanson CJ, Aisen P, et al. *N Engl J Med* 2023;388:9-21.
- [2] Sims JR, Zimmer JA, Evans CD, et al. *JAMA* 2023;330:512-527.

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Correspondence
Shigeki Hirano: s_hirano@chiba-u.jp