Impact of lecanemab on health outcomes in early Alzheimer's disease from a Japanese societal perspective

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Ataru Igarashi[1], Mayaka Tani[2], Mie Kasai Azuma[2], Takuro Utsumi[2], Carolyn Bodnar[3], Se Ryeong Jang[4], Hidetoshi Shibahara[5], Sachie Inoue[5], Oliver Burn[6], Kate Molloy[6], David Trueman[6], Gaku Kamanaka[2], Yuta Kamada[4], Yukinori Sakata[2], Kiyoyuki Tomita[2]

[1]Tokyo University, Tokyo, Japan, [2]Eisai Co., Ltd, Tokyo, Japan, [3]Eisai Europe Limited., Hertfordshire, United Kingdom, [4]Eisai Inc., Nutley, NJ, USA, [5]CRECON Medical Assessment, Tokyo, Japan, [6]Source Health Economics, London, United Kingdom.

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Introduction

Background

- Alzheimer's disease (AD), is the leading cause of cognitive impairment and dementia, is responsible for approximately 60% of all dementia cases worldwide and 67.6% of dementia cases in Japan.
- Lecanemab (LEC) is a humanized monoclonal antibody (IgG1) and the first approved treatment for patients with mild cognitive impairment (MCI) due to AD and mild AD.

Objective

- To estimate the impact of LEC treatment on health outcomes of Japanese patients with early AD (MCI due to AD and mild AD) using a cost-effectiveness model.

Methods: Overview

- A Markov model was developed to estimate disease progression over the lifetime of patients with early AD who received either LEC with standard of care (SOC) or SOC alone.
- The target population consists of Japanese patients with early AD (mean age 71.46 years [1], 68% female [2]).
- The analysis used an effective lifetime horizon of up to 30 years to capture differential outcomes over the lifetime of the individual.

Table 1. Analytical framework

	Target population	Intervention	Comparators
(a)	MCI due to AD	LEC+SOC*	SOC
(b)	Mild AD	LEC + Donepezil + SOC	Donepezil + SOC

* Non-pharmacological treatment includes follow-up and lifestyle advice.
Abbreviations: SOC, standard of care

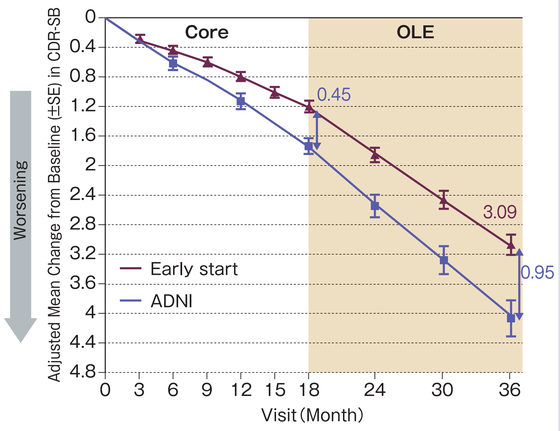
Methods: Clinical parameters

- Transition probabilities during 0-18 months of the Markov model were taken directly from the Clarity AD and were calculated from the baseline and 18 months distribution of patients across each health state [3].
- Beyond 18 months, the hazard ratio of LEC to SOC was 0.704, calculated using 36 months data from the Clarity AD including an open-label extension study and matched cohort data [4,5].
- Natural history data on AD progression after 18 months on SOC were derived from Potashman et al., who reported progression rates for the Aβ-positive cohort based on the National Alzheimer's Coordinating Centre Uniform Data set, a large number of patients from a real-world population in the US [6].
- The analysis considered increased mortality due to AD. The relative effects of mortality, as reported by Takata et al., who examined the relationship between cognitive function and mortality in Japanese AD patients, were applied to the general population life tables in Japan [7,8].
- The discontinuation of lecanemab was assumed to occur due to all-cause discontinuation, as observed in the Clarity AD, when a patient transitioned to the moderate AD health state, or when a patient was institutionalized.

Methods: Clarity AD

- Clarity AD was an 18 months treatment (Core study), multicenter, double-blind, placebo-controlled, parallel group study with open-label extension (OLE) in participants with early AD. Eligible participants were randomized 1:1 across 2 treatment groups (placebo and lecanemab 10 mg/kg biweekly) [9].
- In the 36 months data from the Clarity AD including an OLE study, The difference in mean change from baseline in CDR-SB increased to -0.95 [5].

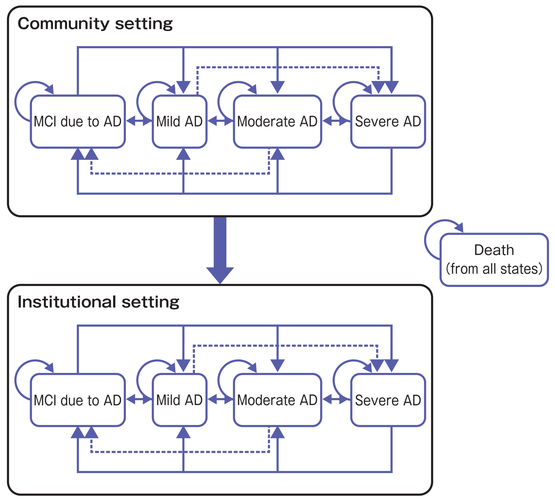
Figure 1. 36 months data from the Clarity AD including an OLE study



Methods: Model structure

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

Figure 2. Model structure



Results: (a) MCI due to AD

- LEC extended the mean time spent in MCI due to AD by 1.31 years (LEC+SOC vs. SOC: 4.99 vs. 3.67) and reduced the time in severe AD, which is associated with high mortality risk, by 0.96 years (2.81 vs. 3.77).
- The overall mean survival time was extended by 0.90 years with LEC (11.29 vs. 10.39).

Figure 3. LEC+SOC and SOC trace by disease severity

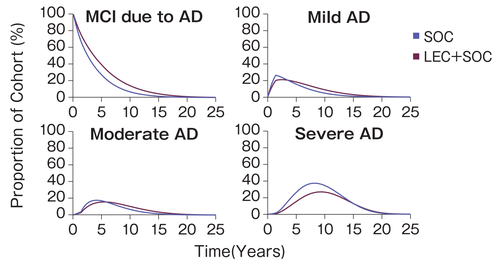
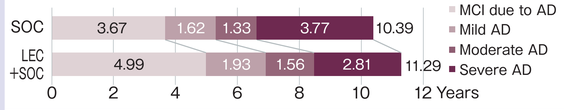


Figure 4. Life years (Mean)



- LEC extended the mean time spent living at home (vs. nursing home) by 1.04 years (10.15 vs. 9.11).
- The mean LEC treatment duration was 4.18 years, when initiated at MCI due to AD stage.

Results: (b) Mild AD

- LEC extended the mean time spent in early AD was extended by 1.09 years (4.38 vs. 3.29), while the time in severe AD was reduced by 0.84 years (3.83 vs. 4.68).
- With LEC the estimated mean survival time was increased by 0.62 years (10.04 vs. 9.42).

Figure 5. LEC+SOC and SOC trace by disease severity

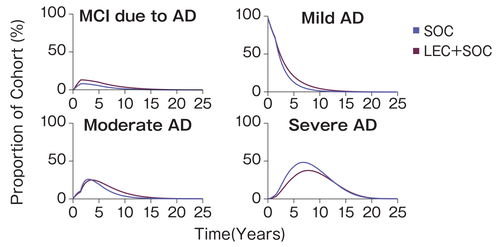
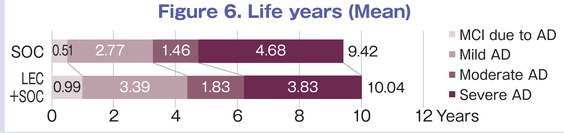


Figure 6. Life years (Mean)



- The mean LEC treatment duration was 2.41 years, when initiated at Mild AD stage.

Discussion

Key Finding

- Our simulations showed that LEC extends the duration of early AD and shortens the duration of severe AD.

Implications

- We believe this may help AD patients maintain a better quality of life and live independently at home for longer.
- In addition, this approach could help reduce the public long-term care cost, which is a growing concern in Japan.

Limitation

- Our model was constrained by the limited long-term efficacy data for LEC treatment. We used disease progression data for LEC and SOC from the core results of the Clarity AD trial for 18 months from the initiation of treatment. Beyond 18 months, disease progression was projected using ADNI data to represent natural disease progression, while the efficacy of LEC was drawn from the latest results available from the OLE period, up to 36 months in the Clarity AD study [10]. Although the OLE data are robust, long-term efficacy data across a lifetime horizon of up to 30 years remain limited. Despite the lack of natural disease progression data specific to the Japanese population, previous studies have suggested a progression comparable to that observed in ADNI data [11].

Conclusion

- LEC delayed disease progression in Japanese patients with early AD, preserving their independence longer compared with SOC.

Reference

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