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The role of trials in health-economic evaluation of anti-amyloid treatment for early Alzheimer’s disease

08.Health economics and clinical trials

Biographies (1 for poster/oral communications & 4 for the symposium) / 150 words per bio

Dr. Ron Handels has obtained his PhD in 2014 on the potential of Alzheimer's disease biomarkers from a health-economic perspective. He continued to focus on health-economic evaluation of biomarkers, disease-modifying treatment and care interventions in in several European projects. He is specialized in cost-effectiveness analysis and operates from a network of health-economists across Europe.

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Abstract:

INTRODUCTION

Health-economic evidence is crucial for decisions on reimbursing anti-amyloid treatment for early Alzheimer’s Disease (AD). Recent phase 3 trials showed significant effects on symptoms over an 18-month follow-up period, leading to regulatory approvals of lecanemab in the United States, Japan and China. Current trial designs do not allow direct assessment of cost-effectiveness of anti-amyloid therapies. A large part of the clinical benefit can be expected to be incurred beyond the period of observation, and trials do not capture effects on resource utilization and care costs, as shown in our previous review [1]. Health-economic simulation models implement trial efficacy evidence, extrapolate over a lifetime period and estimate the associated impact on health-economic outcomes. This modelling relies on key assumptions regarding the sustainability or waning of the treatment effect, as well as how disease progression interacts with mortality. In addition, health-economic outcomes are possibly driven by the design of the diagnostic workup, treatment management method, treatment efficacy in (genetic) subgroups.

We present results from a health-economic evaluation of anti-amyloid treatment based on phase 3 trial efficacy evidence and discuss how to overcome limitations in underlying trial data.

METHODS

We developed an open-source economic model [2] to simulate the lifetime health-economic effects of lecanemab anti-amyloid treatment on reducing disease progression in people with early AD, and its corresponding impact on quality-adjusted life years and care costs in a U.S. setting. The model is available in different formats and can freely be accessed at https://github.com/ronhandels/ipecad. The model was populated with data from the registrational trials of lecanemab.

RESULTS

Anti-amyloid treatment at the current US list price ($26,500) resulted in mean per-person lifetime quality-adjusted life year (QALY) gains (0.35) and care costs savings ($3,095) at additional diagnostic and drug costs ($113,381). Incremental cost-effectiveness ratio (ICER) was $292,650 per QALY gained. Assuming sustained effect and waning improved ICER ($161,696/QALY) and even more when assuming no waning ($85,306/QALY). ApoE4 noncarrier genetic subgroup improved ICER ($213,014/QALY) and ApoE4 carrier had worse ICER ($354,677/QALY).

Blood-based markers can be positions as a screening test only forwarding persons with abnormal amyloid for a follow-up (cerebrospinal fluid (CSF) test or PET scan). This resulted in less required expensive CSF/PET test to identify persons eligible for treatment. However, part of the population was incorrectly labelled as normal amyloid, missing the opportunity to generate the effect of anti-amyloid treatment. A future subcutaneous injection formulation has the potential to reduce treatment administration costs, which contributed a large part of the costs.

DISCUSSION

Our cost-effectiveness estimates for anti-amyloid treatment in early AD may exceed common willingness-to-pay thresholds in the U.S. However, cost-effectiveness estimates improved with the use of blood-based markers and subcutaneous administration. Anti-amyloid treatment is potentially cost-effective in specific subgroups. These results strongly rely on assumptions on extrapolating effects beyond current trial follow-up period. We recommend setting up a registry system to obtain real-world long-term follow-up data on patient-relevant effectiveness outcomes. Such data can be analyzed for optimal subgroups and for the effect of different treatment stopping rules. In addition, real-world evidence collection could be supported by “pay-for-performance” in which payers incur treatment costs proportional to the treatment benefit within an individual.

CONFLICT OF INTEREST STATEMENT

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