Landscape assessment and key HTA considerations in Alzheimer's disease

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Background

Alzheimer's disease (AD) is most common cause of dementia worldwide including Europe.[1] The current therapies offer symptomatic treatment, while the newer therapies under development are disease-modifying drugs (DMD). A number of DMD for AD are under development though none has been to the market yet.[2] The newer DMD target earlier disease stages compared to currently available therapies, and therefore, the existing health technology assessment (HTA) experience will have limited applicability. The current study aimed to undertake a landscape assessment of newer therapies being evaluated in AD and assess positioning of ongoing clinical trials to evolving HTA evidence needs.

Methods

Clinicaltrials.gov were searched for interventional trials in AD with recruitment status as, not yet recruiting, recruiting, enrolling, and active trials for last 10 years. The search hits obtained were screened to include ongoing studies evaluating therapies for AD, irrespective of the mechanism of action. Clinical trials evaluating diagnostic techniques were not included. The studies deemed eligible for inclusion were segregated based on type of intervention evaluated (AchIs, DMDs, cognitive enhancers, transcranial therapies, or agents relieving symptoms like anxiety and depression).

A review of literature was also undertaken for identifying studies reporting HTA considerations in AD. Searching of Embase® was undertaken using keywords like Alzheimer's disease, Health technology assessments, market access, HTA considerations, reimbursement, and there variants. In total 849 records were retrieved from the searches. These records were screened based on title and abstracts for identifying studies describing evidence needs for HTA submissions in AD. Following the first stage screening 10 studies were included for detailed second stage screening based on full-text publications. Following the screening of full-text publications, eight studies were included.

Results

Searching of clinicaltrial.gov identified a total of 150 clinical trials of which ~50% evaluated DMD, while remaining evaluated cognitive enhancers, transcranial therapies, or agents relieving symptoms like anxiety and depression (Figure 1).

Twenty-six DMD were evaluated in early/mild AD (26 agents) with 10 agents in late stage phase II/III trials expecting launch by 2025 and 5 agents (TRx0237, E2609, ALZT-OP1, Crenezumab, and Gantenerumab) expecting launch by 2021 (Figure 2). Impact on cognition was the majorly assessed outcome (using ADAS-Cog and MMSE) followed by QoL and functionality outcomes. Nearly 50% of DMD trials evaluated QoL, however, caregiver QoL assessment was limited (4 trials). Similarly, limited (five) trials assessed resource utilization and correlation between disease stage and outcomes.

Of 849 hits obtained searching literature for AD HTA considerations, 8 studies were included following detailed assessment. Six of the eight publications reported results from the ROADMAP project, while two studies reported new drug regulations in France and its impact on the market access.[3] The publications for the ROADMAP reported discussions and activities of the regulatory and HTA expert advisory group of the ROADMAP (real-world outcomes across the Alzheimer's disease spectrum: a multimodal data access platform) project.[4] According to the publication, the goal of this project was to provide sufficient evidence-base to facilitate rapid decision making by HTA bodies and regulators. The ROADMAP reported partial applicability of existing HTA experience to the reimbursement of newer therapies. According to the authors, health-related QoL was critical from the HTA perspective besides the need for validated and accepted outcomes for HTA process particularly for capturing the early stages of AD, including prodromal disease and mild cognitive impairment.

Our evaluation of ongoing trials retrieved through searching of clinicaltrials.gov against recommendations proposed in the ROADMAP publications indicated the use of validated outcomes across ongoing trials. The majority of measures used in trials assessed cognition and QoL through use of validated outcomes. However, evidence needs for modelling assumptions like correlation between disease stages and outcomes, resource utilization, and caregiver QoL were less frequently addressed. This indicated towards the need of real-world evidence to better characterize the impact of DMD on these parameters for adequately addressing the HTA needs.

Figure 1: Overview of ongoing clinical trials assessing DMD in AD

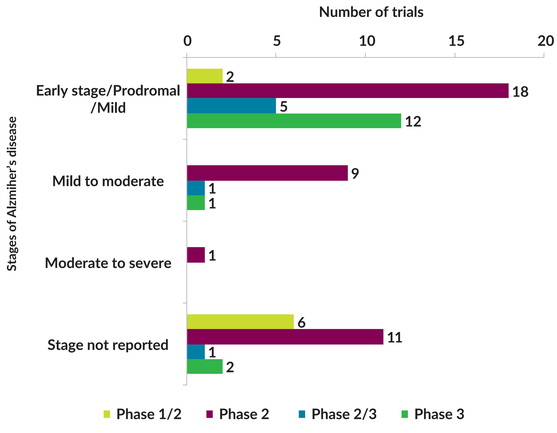
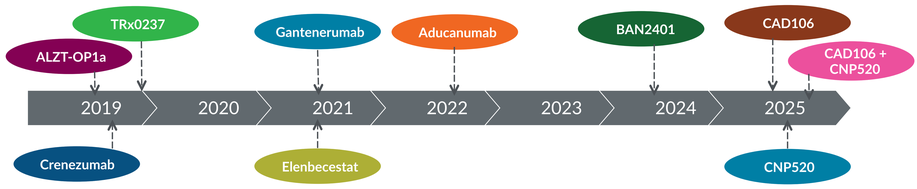


Figure 2: Pipelines of DMD in Alzheimer's disease early stages



Conclusions

- A number of DMD for early stage Alzheimer's are being evaluated in late phase clinical trials with an expected launch in next 5 years
- These trials majorly assess impact on cognition (using ADAS-Cog and MMSE) followed by QoL, and functionality outcomes using validated outcomes, in-line with the evolving HTA needs in AD
- However, only limited number of trials are evaluating caregiver QoL and correlation between disease stage and outcomes which is critical to the HTA process. Therefore, real-world evidence will be needed to better characterize the impact DMD will have on caregiver QoL, resource utilization, and correlation between disease stage and outcomes

References

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AchIs: Acetyl cholinesterase inhibitors; ADAS-Cog: Alzheimer's Disease Assessment Scale-cognitive subscale; MMSE: Mini-Mental State Exam; QoL: Quality of Life; ROADMAP: Real-world outcomes across the Alzheimer's disease spectrum: a multimodal data access platform

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