Potential Meaningful Benefit of Anti-Amyloid Treatments for Early Stages of Alzheimer's Disease (AD)

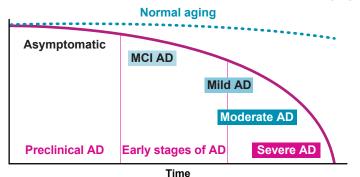
AD IS A CHRONIC PROGRESSIVE DISEASE THAT ACCELERATES AFTER EARLY STAGES

Hypothetical Model of Decline Across the AD Continuum Versus Normal Aging^{1,2}

Cognition and

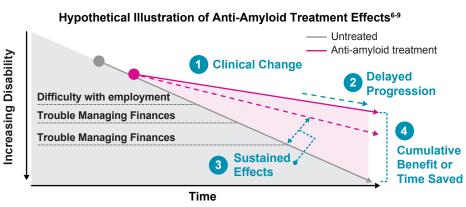
Function

Decreasing



Due to the neurodegenerative nature and accelerating progression in later stages of AD, early intervention is crucial³⁻⁵

ANTI-AMYLOID TREATMENTS MAY PROLONG TIME SPENT IN THE EARLY STAGES OF AD



Anti-amyloid treatments affect AD pathophysiology by targeting specific amyloid beta species¹⁰

1	Clinical Change	Improvement or stabilization of clinical symptoms ¹¹
2	Delayed Progression	Slowing of cognitive and functional decline, which is reflected in a change in the rate or slope of decline ⁷
3	Sustained Effects	Symptom differences between treated and untreated individuals persist even after discontinuing treatment, suggesting disease modification ¹¹
4	Cumulative Benefit	There is a gradual accumulation of treatment effects over time such that the treatment effects increase with longer therapy duration ⁷

THERE IS A NEED FOR OUTCOMES THAT REFLECT THE MEANINGFUL BENEFITS OF TREATMENTS TARGETING PATHOLOGY IN EARLY STAGES OF AD

The Clinical Dementia Rating – Sum of Boxes (CDR-SB) is an inherently clinically meaningful outcome for early stages of AD^{12,13}



It **assesses subtle changes** in cognition and function in early stages^{12,13}



It is a **continuous measure** that is sensitive to change over time^{12,13}



Any increment of change on an individual domain of the CDR-SB (0.5 or 1) is considered **clinically meaningful** for an individual⁸





RELATING THE CDR-SB TO FUNCTIONAL CHANGES CAN HELP ESTIMATE THE TIME TO LOSS OF INDEPENDENCE WITH AD TREATMENTS

Hypothetical Example of the Relationship Between CDR-SB and Functional Outcomes, and Longevity of Independence Due To Anti-Amyloid Treatment¹⁴

A 20% to 30% slowing of AD in early stages could mean a delay in onset of a later stage⁸

Functional outcomes

Anti-amyloid treatment

- · Fully independent in BADL
- · Independent in IADL
 - Difficulty with meal preparation
- · 40 months to loss of



- functional independence
- · Fully independent in BADL
- · Independent in IADL
 - Difficulty remembering dates and medications
- · 29 months to loss of functional independence



This is a hypothetical example based on data modeling, actual results in clinical practice may vary. The potential to preserve independence may be reviewed as part of a thorough discussion on the risks and benefits of anti-amyloid treatments for appropriate individuals¹⁴

SUMMARY: MEANINGFUL BENEFIT OF ANTI-AMYLOID TREATMENTS FOR EARLY STAGES OF AD



Anti-amyloid treatment should be initiated in early disease stages to maximize time saved or prolong delay in decline³⁻⁵



Baseline

CDR-SB 1

Baseline

CDR-SB 2

Due to the potential for cumulative benefit, the meaningful benefit of anti-amyloid therapies is expected to increase with increased therapy duration7,8



Ongoing AD neurodegeneration may be driven by pathological changes beyond detectable amyloid plaques, necessitating continued anti-amyloid treatment to observe cumulative benefit over time10,15-17



Anti-amyloid treatments should also be evaluated for indirect benefits such as their broad health and financial impacts on patients, families, payers, and society18

ABBREVIATIONS

AD, Alzheimer's disease; BADL, basic activities of daily living; IADL, instrumental activities of daily living.

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