BACE Inhibitors

DRIVER PROJECT · BIOLOGICAL PATHWAYS & TRIALS

Alzheimer's Disease Data Initiative

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Did BACE inhibitor dosing drive cognitive decline — and could alternative dosing enable safer early intervention?

Leveraging BACE inhibitor trial data to evaluate early treatment effects and inform more effective Alzheimer's prevention and trial design.

A cross-trial reanalysis drawing on

10+

BACE and γ-secretase inhibitor trials, harmonized together*

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secure environment — AD Workbench — for reproducible analysis

» The unresolved question

BACE inhibitor trials were halted for lack of efficacy or adverse outcomes, leaving open questions about timing, patient selection and mechanism.

» Why reanalysis matters

Historically each trial was analyzed in isolation. Harmonizing data across trials enables a more complete evaluation of treatment effects in early-stage populations.

» How the work runs

A consortium of academic, nonprofit and industry partners analyzes data inside AD Workbench — reproducible workflows without moving sensitive data.

Key research questions

- Is the cognitive decline on-target (Aβ-related) or off-target?
- If off-target, can molecules or populations be optimized?
- If on-target, is there a dose that is both effective and safe long-term?

What this could reveal

On- vs off-target

Whether observed cognitive decline is an on-target (Aβ-related) or off-target effect.

Optimization

Whether molecules or populations can be optimized to mitigate cognitive worsening.

Safe dosing

Whether a level of BACE inhibition is both effective and safe for chronic dosing.

Co-led by Drs. Paul Aisen (USC ATRI) and Robert Vassar (Northwestern Feinberg), with a steering committee spanning DZNE/TUM, USC, Northwestern and the Alzheimer's Association. Hosted on AD Workbench by the AD Data Initiative. *Trial count pending SME confirmation.