Form A4a:
AD-specific treatments

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Disclosures: Suzanne Schindler, MD, PhD

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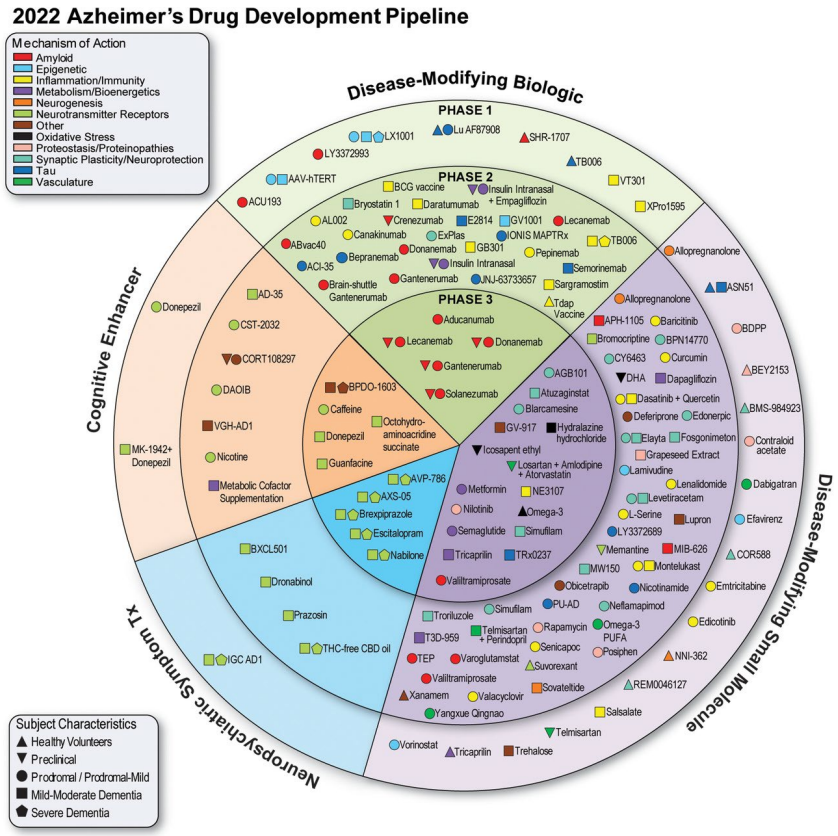
- **Dr. Schindler has previously analyzed biomarker data provided to Washington University by C2N Diagnostics and Roche Diagnostics; no financial incentives or research funding were provided to Dr. Schindler in return.**
- Stock/Equity: None
- **Consulting/Employment: Dr. Schindler served on a scientific advisory board for Eisai**
- Speakers Bureau/Honoraria: Dr. Schindler receives honoraria as a member of the biorepository review committee for the non-profit National Centralized Repository for Alzheimer's Disease (NCRAD); she has received honoraria for participating in expert panels and reviewing grants from non-profit organizations
- Other: Dr. Schindler previously served as a sub-PI for the A4, DIAN-TU, and ENGAGE trials. Dr. Schindler participated in the IDEAS trial.

Proliferation of AD-specific treatments

- Aducanumab received accelerated FDA approved in 2021, but was never widely used
- Lecanemab received full FDA approval on July 6, 2023 and is in clinical use
- Additional AD-specific treatments may be approved within the next year
- In 2022 there were 143 agents in 172 AD clinical trials*
- Currently recruiting trials require 50,575 participants
- Some treatments have major effects on ADRD biomarkers
- Some of our research participants are receiving these treatments



* Cummings et al., *Alzheimer's and Dementia* 2022

Why do we need a new form?

- There has been no uniform mechanism to identify participants who have received treatments that modify ADRD biomarkers
- Treatments that effect ADRD biomarkers and cognitive performance could confound analyses
- Limitations of the medication form:
  - Records medications at the time of administration, but does not include transient treatment (e.g., 6 months of treatment with lecanemab in-between study visits)
  - Not designed to capture participation in clinical trials, in which the treatment may or may not be known (e.g., placebo or active treatment)
  - Does not capture any drug effects related to treatments (e.g., ARIA) that can affect ADRD biomarkers (e.g., brain MRI)
- AD-specific treatments and trials are rapidly evolving, and a separate form provides increased flexibility for frequent changes

Process for creating form

- Key considerations:
  - Burden on participants and centers
  - Respecting contracts with pharmaceutical companies
  - Alignment with other constructs (e.g., CADRO classification)
  - Flexibility
- Sub-group of CTF Clinical Measures and Diagnosis Workgroup met and generated a first draft
- The CTF Clinical Measures and Diagnosis Workgroup discussed the draft form and made revisions
- Feedback was elicited from all the centers (April 22, 2022) and incorporated into a revised draft
- The form will primarily be used to identify individuals with data that may be confounded by AD-specific treatments, not to provide detailed information for analysis of AD-specific treatments

Question #1

Has the participant ever been prescribed or been enrolled in a clinical trial of a treatment expected to modify ADRD biomarkers?

❑Yes/No/Unknown

If no, end of form

Question #2

Please provide information about the clinical treatment(s) and/or trial(s):

Primary Drug Target *(check all that apply)*	**Specific treatment and/or trial**	**Start date** *(month/year)*	**End date** *(month/year)*	**How was the treatment provided?**	**If clinical trial, in which group was the participant?**
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____ *ALZNET:* _____	__ __ / _ _ _ _	__ __ / _ _ _ _	☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown

Question #3

Has the participant ever experienced amyloid related imaging abnormalities-edema (ARIA-E), amyloid related imaging abnormalities-hemorrhage (ARIA-H), or other major adverse events associated with treatments expected to modify ADRD biomarkers?

- ❑Yes/No/Unknown

What major adverse events associated with treatments expected to modify ADRD biomarkers did they experience? (check all that apply)

- ❑Amyloid related imaging abnormalities-edema (ARIA-E)
- ❑Amyloid related imaging abnormalities-hemorrhage (ARIA-H)
- ❑Other issues (free text)

Future of the form

- The major use will be to identify individuals who have received treatments that confound biomarker analyses
- It is likely that the form will be revised often, especially if new drugs are approved
- If a larger proportion of participants start taking AD-specific treatments, a greater level of detail (e.g., doses, more details about adverse effects) may be appropriate to add

Thank you!

The CTF Clinical Measures and Diagnosis Workgroup

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