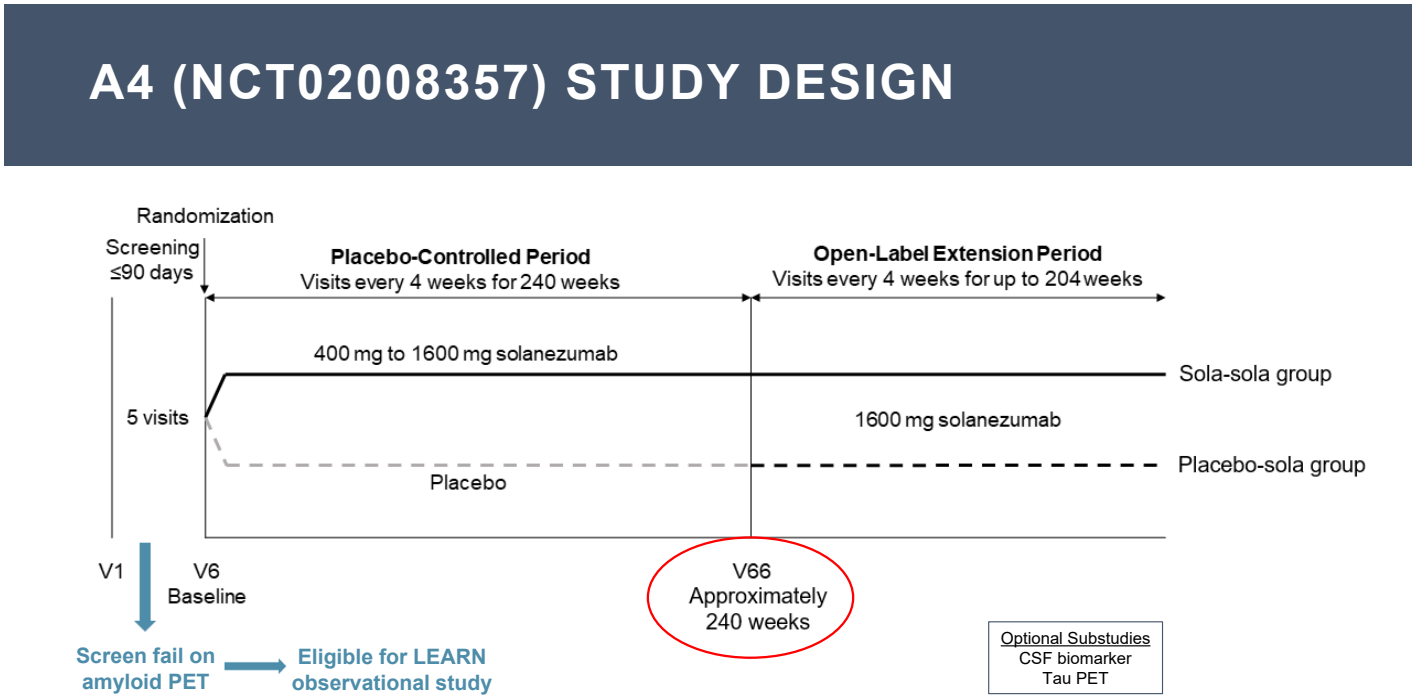
Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study Results Summary

Selected Slides from the Presentation of the A4 Study at the Alzheimer Association International Conference
17 July 2023

The A4 Study included people who had eligible amyloid PET scan results, randomly assigned to get solanezumab or placebo for 240 weeks (about 4.5 years). Study participants who finished the first part of the study were invited to enter the open-label extension period, when everyone got solanezumab.

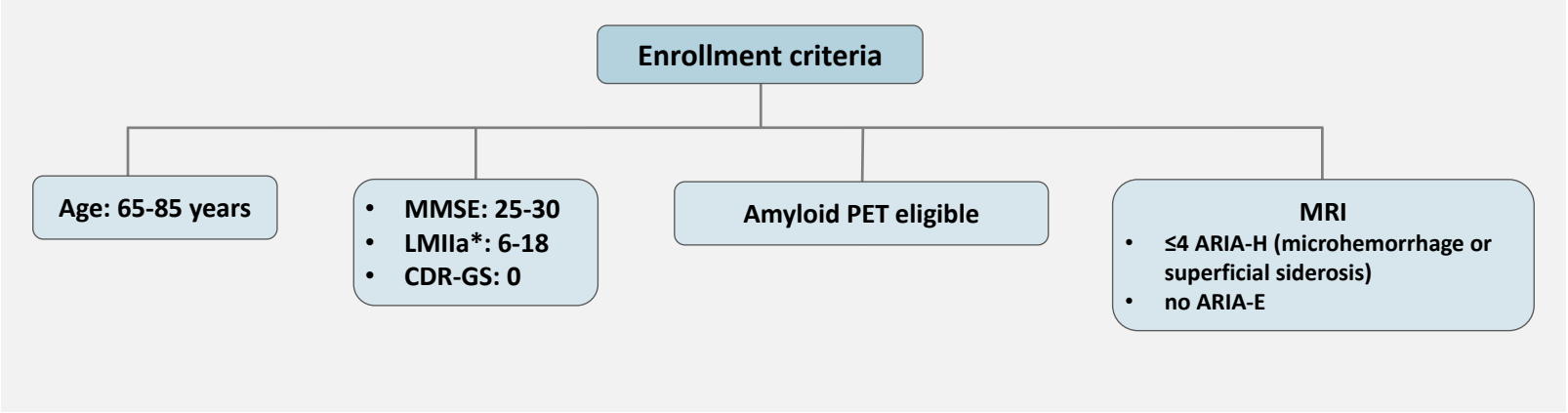
People who had ineligible amyloid PET scan results were invited to enter the Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) observational study.



Abbreviations: CSF=cerebrospinal fluid; PET=positron emission tomography; LEARN=Longitudinal Evaluation of Amyloid Risk and Neurodegeneration; v=visit

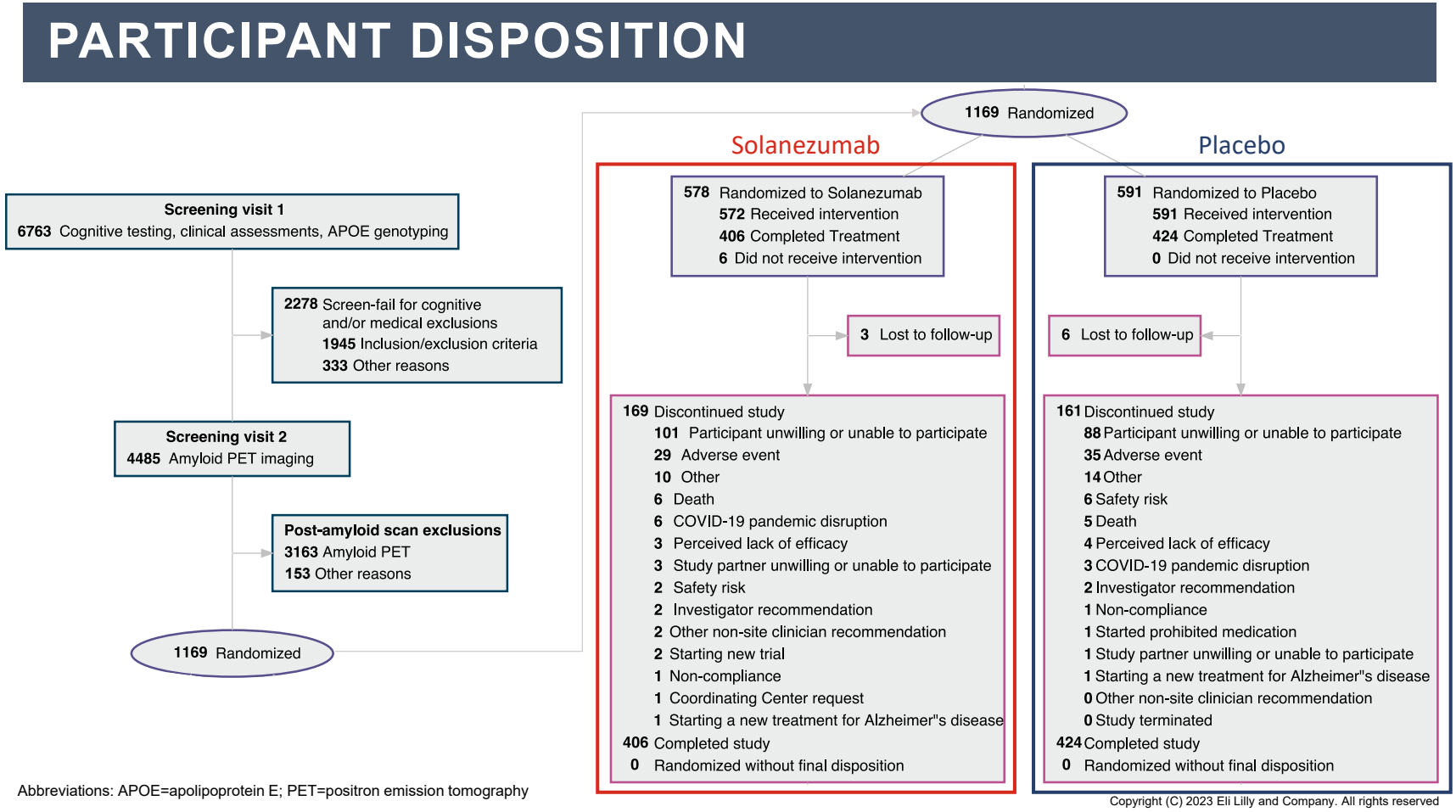
Characteristics of people who were eligible to enter the A4 study are described here:

KEY INCLUSION CRITERIA



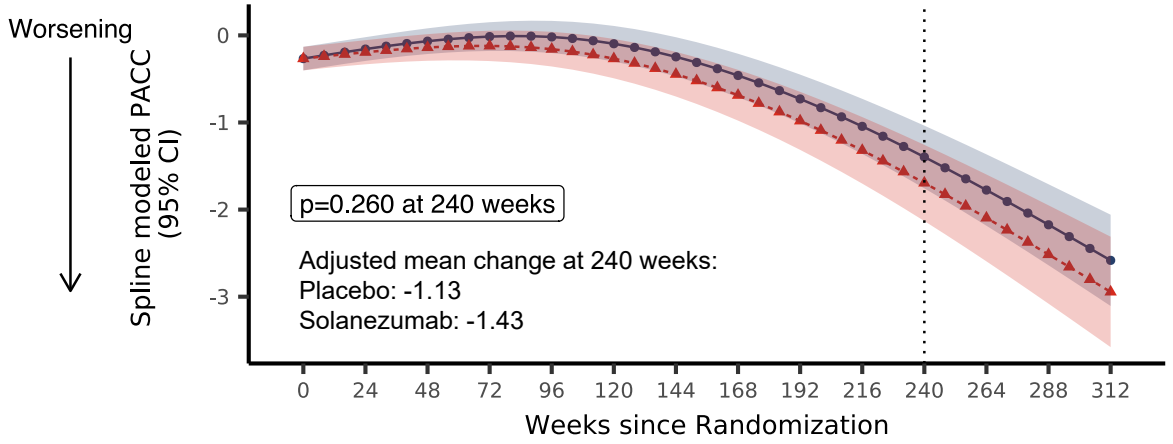
* subtest from the Wechsler Memory Scale
Abbreviations: ARIA-E=amyloid-related imaging abnormalities-edema/effusions; ARIA-H=amyloid-related imaging abnormalities-hemorrhage/hemosiderin deposition; CDR-GS=Clinical Dementia Rating-global score; LMIIa=Logical Memory IIa; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; PET=positron emission tomography

The number of participants at various points in the A4 Study screening and after randomization, to either solanezumab or placebo, during the double-blind phase are shown here:



This slide shows the results from the primary outcome of the A4 Study – the Preclinical Alzheimer Cognitive Composite (PACC) – composed of four memory and thinking tests. There was no difference in the rate of cognitive decline between those participants randomized to solanezumab (red) or placebo (blue).

NO SIGNIFICANT DIFFERENCE OBSERVED ON THE PRIMARY OUTCOME (PACC) DOUBLE-BLIND PERIOD



No. of Participants

Solanezumab	564	554	534	518	498	484	432	426	400	372	355	156	15	2
Placebo	583	569	555	532	510	490	438	427	407	392	363	176	13	

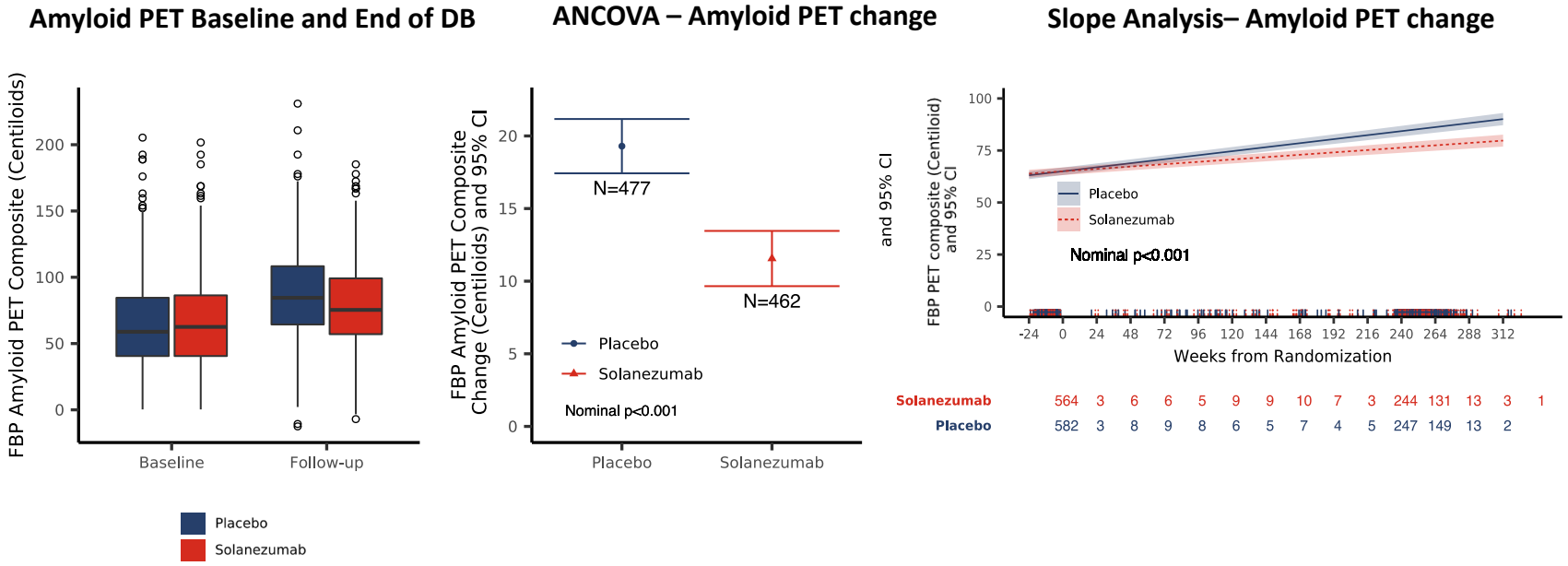
PACC components:

- FCSRT-96
- Delayed Recall on the LMIIa*
- DSST#
- MMSE

* subtest from the Wechsler Memory Scale; # from the Wechsler Adult Intelligence Scale-Revised
Abbreviations: CI=confidence interval; DSST=Digit Symbol Substitution Test; FCSRT-96=Free and Cued Selective Reminding Test 96; LM=Logical Memory; PACC=Preclinical Alzheimer's Cognitive Composite; MMSE=Mini-Mental State Examination

This slide shows the amyloid PET levels at baseline and at the end of the double-blind phase (approximately 4.5 years) in the group who was randomized to solanezumab (red) or placebo (blue). The solanezumab group has slightly less increase in amyloid than the placebo group, but both groups showed an increase on amyloid PET over the 4.5 years.

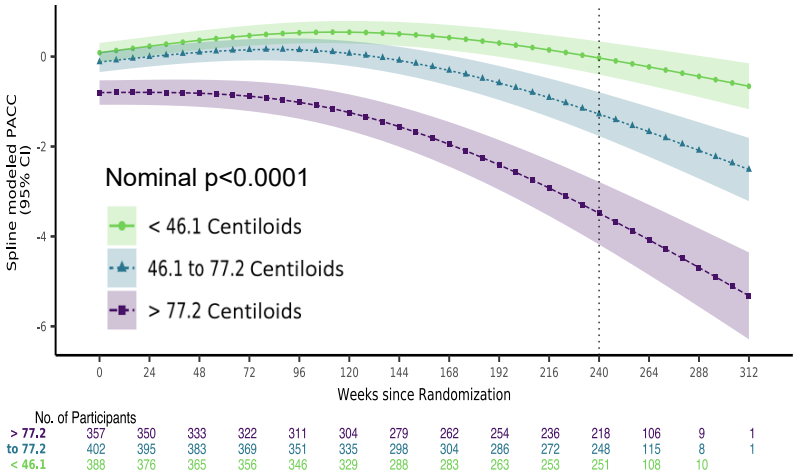
AMYLOID PET INCREASED IN BOTH TREATMENT GROUPS LESS IN SOLANEZUMAB GROUP



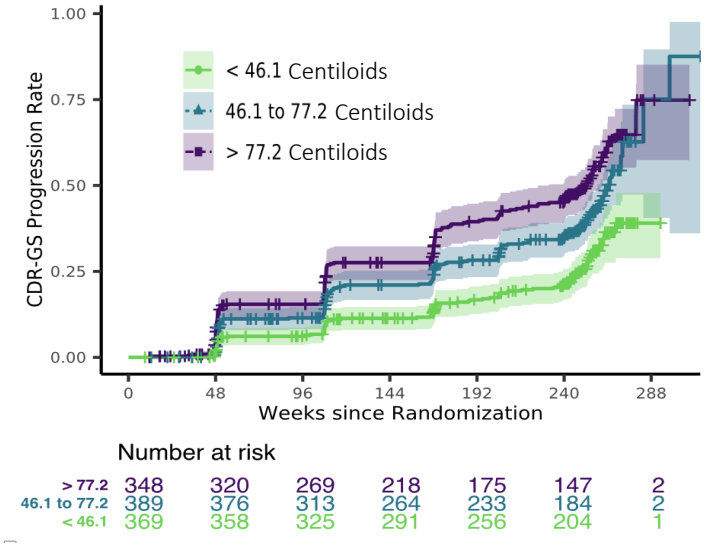
This slide shows the effect of baseline amyloid levels (from the screening amyloid PET scan) on cognitive decline (PACC shown on the left) and likelihood of progression to higher level of functional impairment on the Clinical Dementia Rating Scale (CDR) Global Score. The colors show the tertiles (dividing the group into thirds) based on the level of amyloid on the PET scan. The highest level of baseline amyloid (purple) showed the fastest decline and highest likelihood of progression.

BASELINE AMYLOID EFFECTS ON PACC DECLINE AND TIME TO CDR-GS PROGRESSION (TERTILE ANALYSES A4 POOLED ARMS)

Preclinical Alzheimer Cognitive Composite (PACC)



Progression to CDR Global > 0



Post hoc analysis of combined treatment-group data.
Dashed line at 240 weeks indicates planned final visit timing, which occurred later for some participants due to COVID-19 pandemic.

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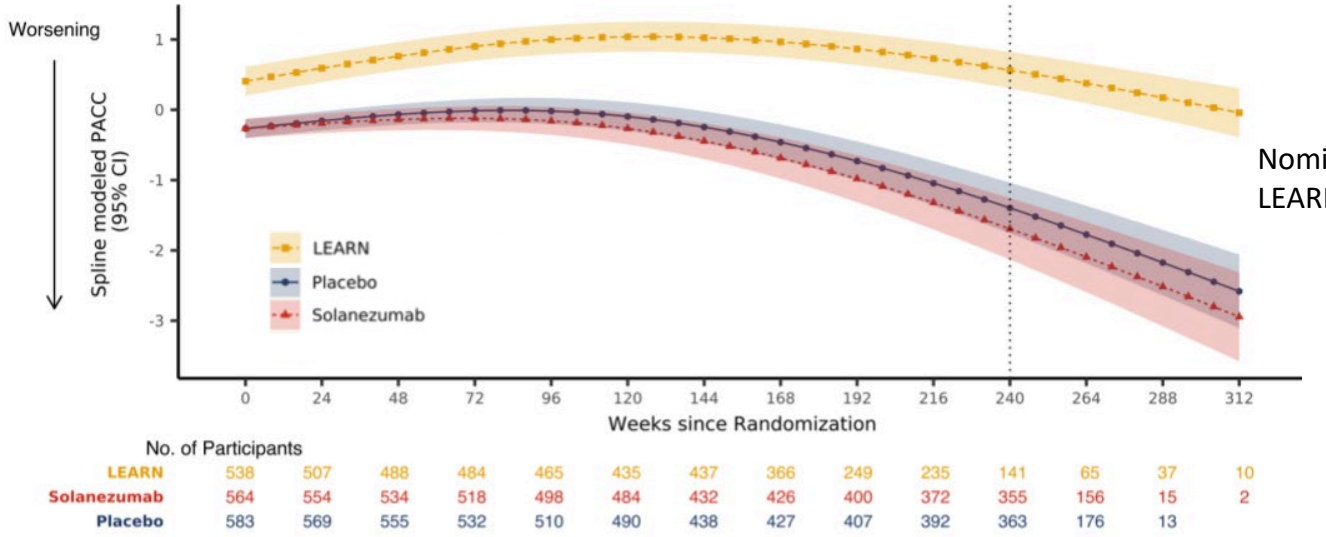
This slide compares the LEARN Study cohort (who did not show elevated amyloid at baseline) to the two A4 Study treatment arms (both groups with elevated amyloid at baseline) on the PACC. The LEARN Study group did not show cognitive decline on the PACC, compared to the cognitive decline observed in both of the A4 groups with elevated amyloid.

NO PACC DECLINE OBSERVED IN LEARN IN CONTRAST TO A4 TREATMENT ARMS

Preclinical Alzheimer Cognitive Composite (PACC)



Nominal p<0.001
LEARN vs. A4 Placebo

Mean (95% CI) derived from spline model of Preclinical Alzheimer's Cognitive Composite (PACC).

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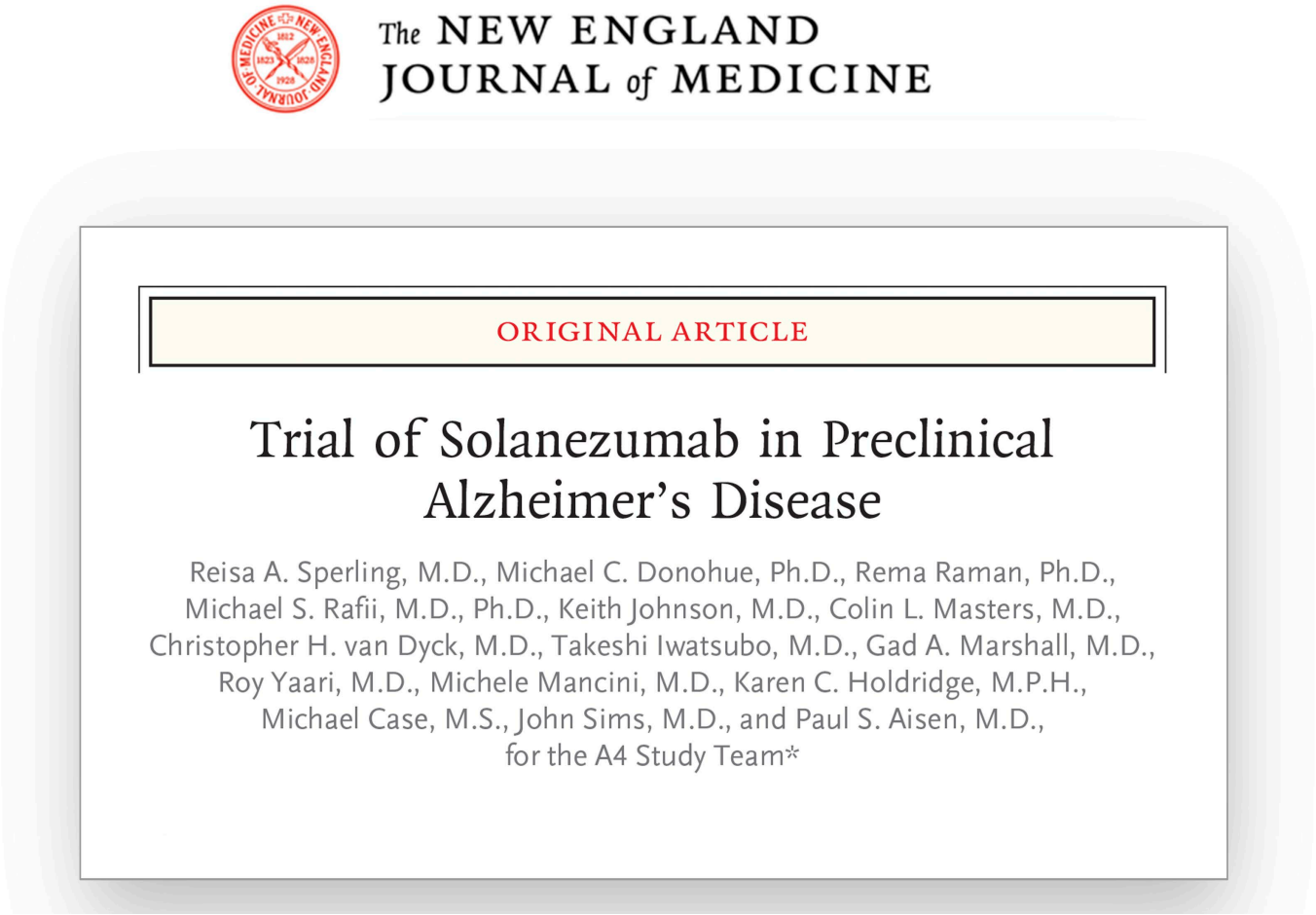
The A4 Study is featured as an article in the New England Journal of Medicine, published online July 17, 2023.
Link to article: HTTPS://dx.doi.org/10.1056/NEJMoa2305032. If you don't already have an account with the New England Journal of Medicine, you can scroll down the page from the link above and join at no cost so you can have access to the full A4 Study article.



This slide expresses our gratitude to the very dedicated A4 Study and LEARN Study participants without whom these important studies and advancing knowledge would not be possible.

ACKNOWLEDGMENTS

First and Foremost:
The A4 and LEARN Participants
and Study Partners

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