ALTITUDE-AD: Cost Savings Using a pTau217 Screening Assay in an Ongoing Phase 2 Study of Sabirnetug in Early Alzheimer's Disease

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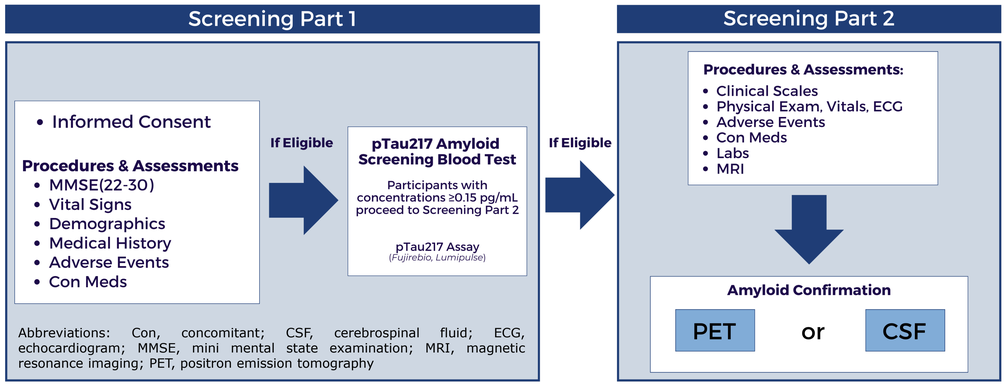
Background

- Early detection of Alzheimer's disease (AD) is challenging, and screening for AD clinical trials requires burdensome positron emission tomography (PET) scans and lumbar punctures (LPs) for CSF collection
- In the phase 1 INTERCEPT-AD study of sabirnetug (ACU193),[1] 60% of amyloid PET scans at screening were negative
- pTau217 plasma concentrations are highly predictive for AD pathology[2]
- A plasma pTau217 assay could be used as an enrichment strategy at screening to help identify potential participants with a high likelihood of meeting amyloid inclusion criteria on PET or cerebrospinal fluid (CSF) amyloid-beta ($A\beta)_{42/40}$ ratio
- Screening with plasma pTau217 could reduce the burden to study participants by avoiding unnecessary LPs and radiation exposure from PET scans
- This screening approach can also benefit clinical trial sites by saving them time and resources
- In addition, study sponsors could experience significant cost savings
- We conducted analyses to determine the effect of pTau217 screening on participant enrollment and screening costs

Methods

- ALTITUDE-AD is an 80-week, global, randomized, double-blind, placebo-controlled phase 2 study of sabirnetug in individuals with early symptomatic AD and evidence of amyloid pathology
- The Fujirebio Lumipulse© G pTau217 research-use-only assay was used in North America (US and Canada) as an enrichment strategy during screening to help identify potential participants with a high likelihood of meeting amyloid inclusion criteria using PET or CSF $A\beta_{42/40}$
- Screening occurred in two parts (**Figure 1**)

Figure 1. ALTITUDE-AD Screening Visits and Related Procedures



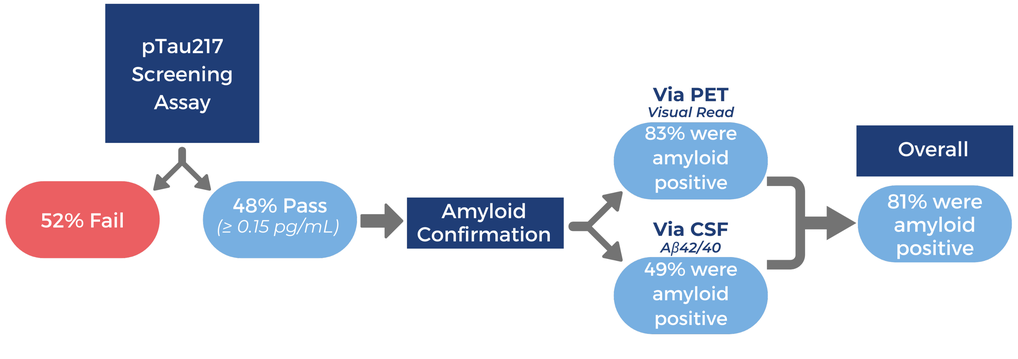
Abbreviations: Con, concomitant; CSF, cerebrospinal fluid; ECG, echocardiogram; MMSE, mini mental state examination; MRI, magnetic resonance imaging; PET, positron emission tomography

Percent Cost Analyses

- Total cost for the 2-part screening was calculated for US and Canadian sites and compared with projected costs if the pTau217 assay had not been used
- Total cost for screening visit 1 includes costs for all procedures and assessments shown Figure 1 part 1, including the pTau217 amyloid blood test
- Total cost for screening visit 2 includes costs for all procedures and assessments shown in Figure 1 part 2, including amyloid confirmation procedures (either PET or CSF)
- Cost savings were determined based on a weighted average of participants screened in North American sites
  - Each site was assigned a weight determined by the number of participants screened
  - The weighting assigned was then multiplied by the cost of the visit and/or procedure, to determine an overall cost per visit

Results

Figure 2. pTau217 Screening Increased the Likelihood of Positive Amyloid Results on PET or CSF



Results (continued)

Figure 3. pTau217 Screening Saved 43% in Overall Screening Costs

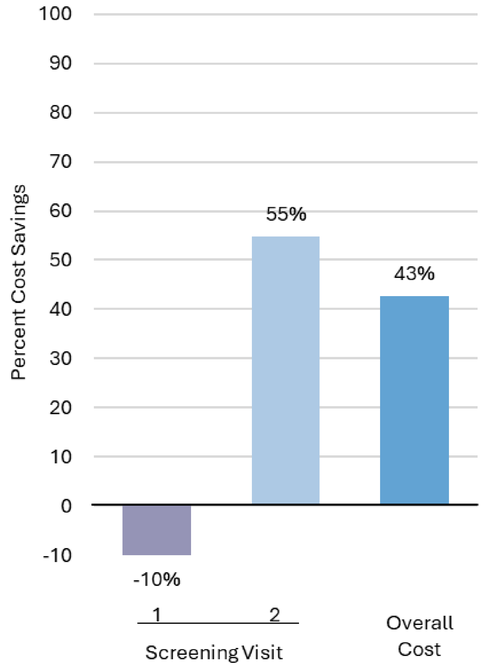
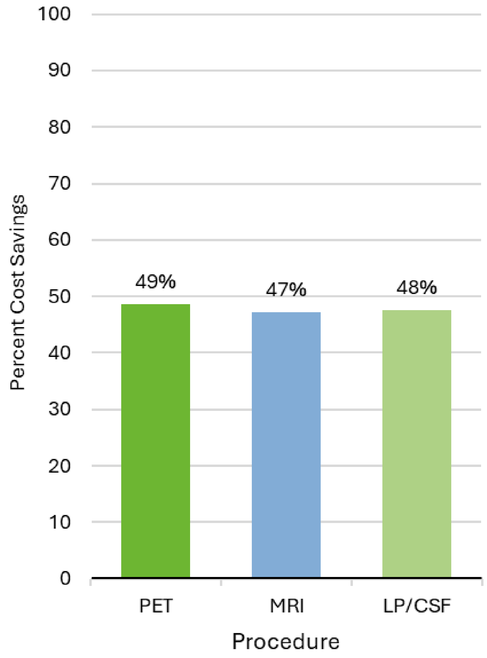


Figure 4. pTau217 Screening Cut the Cost of Key Screening Procedures Almost in Half



Abbreviations: CSF, cerebrospinal fluid; LP, lumbar puncture; MRI, magnetic resonance imaging; PET, positron emission tomography

When compared to estimated costs of screening without the pTau 217 assay (**Figure 3**),

- Cost of screening visit 1 was 10% higher with the cost of the pTau217 assay included
- Cost of screening visit 2 was more than 50% less
- Overall cost savings were 43%

Total costs of procedures (PET, CSF/LP, and magnetic resonance imaging [MRI]) decreased by almost 50% (**Figure 4**) because more than half of potential participants had pTau217 <0.15 pg/mL and therefore did not proceed to screening visit 2.

RESEARCH HIGHLIGHTS

- Screening potential study participants with a plasma pTau217 assay increased the likelihood that participants who underwent LP for CSF $A\beta_{42/40}$ testing or PET would meet amyloid inclusion criteria, resulting in an estimated overall screening cost savings of more than 40%
- More than half of potential participants had pTau217 values <0.15 pg/mL and thus avoided unnecessary LPs and radiation exposure from PET scans
- Further, pTau217 screening saved time and reduced burden for study participants, study sites, and the sponsor

References

1. Siemers E, et al. *J Prev Alzheimers Dis*. 2025;12(1):100005. doi:10.1016/j.tjpad.2024.100005
2. Ashton NJ, et al. *JAMA Neurol*. 2024;81(3):255–263. doi:10.1001/jamaneurol.2023.5319

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Conflicts of Interest: All authors are employees of or consultants for Acumen Pharmaceuticals, Inc and have minor equity interest in Acumen