

Clinical and Amyloid Screen Failure Rates in Episodic Memory Measures of Early AD Trials

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INTRODUCTION

- Episodic memory tests are commonly used in trials of early-stage Alzheimer's disease (AD), in order to verify memory impairment and reduce the rate of amyloid screen failure in trials that involve anti-amyloid therapies that require evidence of cerebral amyloid for enrollment¹.
- Little evidence exists to support the choice of any specific episodic memory test over another for this purpose. The common cutoff to establish the presence of memory impairment is performance of one standard deviation (or lower) below age-based norms. Key factors for study efficiency with respect to this inclusion criterion are screen fail rates on the episodic memory measure and subsequent screen fail rates on amyloid testing.
- The present study examined two episodic memory measures – the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)² and the Cogstate International Shopping List Test (ISLT)³ – to compare their clinical and amyloid screen failure rates in early AD trials.

RESULTS

- The overall clinical screen fail rates were comparable between the two memory measures, with 30% and 33% for ISLT and RBANS, respectively. This is despite the fact that the ISLT allowed for inclusion if just one of two scores met criteria, whereas the RBANS had a single cutoff for inclusion.
- On amyloid PET, there were significant differences between the two measures, with RBANS lower screen failure rate (30%) compared to ISLT (46%); (Figure 1) [$X^2=120.9$, $p < 0.01$].
- Using these results to model enrollment, for every 100 subjects screened with the ISLT, 70 would proceed to amyloid testing, and 38 would be amyloid positive. For the RBANS, 67 would proceed to amyloid testing and 47 would be amyloid positive.

CONCLUSION

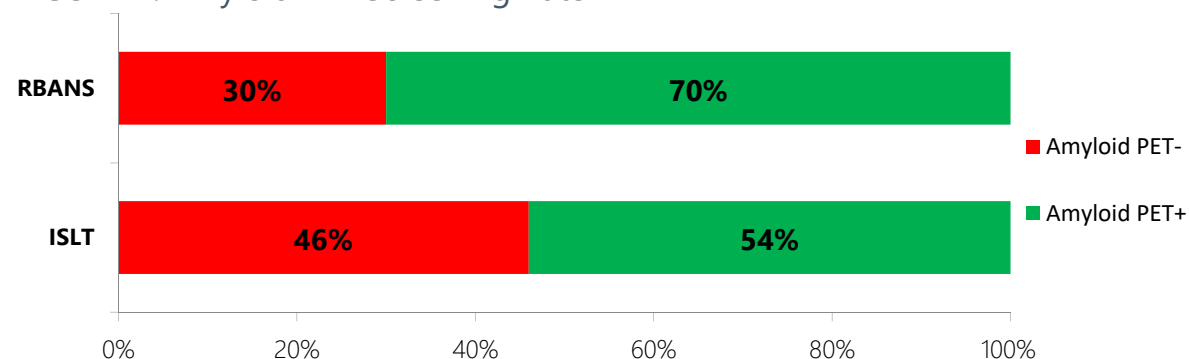
- These two episodic memory measures had similar screen fail rates for subjects across these five trials, but the RBANS DMI appears to be significantly more predictive of cerebral amyloid burden. The fact that the two measures had comparable intrinsic screen fail rates suggests that the cutoff scores were comparable.
- One possible explanation for this finding is that the RBANS DMI is an index score composed of four separate delayed memory recall/recognition subtests, improving the reliability of the score in the measurement of anterograde memory.
- Use of the RBANS in comparison to the ISLT is likely to significantly speed enrollment compared to the ISLT in trials requiring evidence of cerebral amyloid burden.

METHODS

- 13,260 RBANS and 4,401 ISLT assessments from five industry-sponsored clinical trials in AD, including prodromal and early stage mild dementia, were collated for analyses.
- The percentages of participants that did not meet inclusion criteria (clinical screen failure rates) on each of the episodic memory measures were calculated. For those that met all inclusionary criteria and proceeded to PET imaging, the amyloid screen failure rates were also computed and compared between the two measures.
- In all studies, scores had to fall one standard deviation or lower for inclusion. The RBANS Delayed Memory Index (DMI) was the inclusion measure for that scale, with scores of 85 or lower meeting criteria. For studies using the ISLT, inclusion criterion would be met with a z-score of -1.0 or less on either the sum or the learning trials or the delayed free recall trial.

- Extrapolating to a trial that intended to enroll 1,000 subjects, using the ISLT would require screening 2,646 subjects with the ISLT for 1,852 subjects meeting ISLT criteria, followed by 852 amyloid screen failures. Using the RBANS would require screening 2,133 subjects with the RBANS for 1,429 subjects meeting RBANS criteria, followed by 429 amyloid screen fails.

FIGURE 1: Amyloid PET Screening Rate



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