**Introduction**

- The elenbecestat MissionAD phase 3 studies assess the effects of BACE inhibitor elenbecestat on clinical and biomarker outcomes in subjects with early Alzheimer’s Disease (AD).
- Entry into the elenbecestat studies requires subjects to show impairment on the immediate or delayed recall components of the International Shopping List Test (ISLT).
- The ISLT is a supervisor administered three-trial verbal list learning test where individuals learn a shopping list of 12 food items. The ISLT has been validated in both mild cognitive impairment (MCI) and AD.
- Prescreening assessments have been considered for use in clinical trials to determine whether a subject is considered a good candidate for more comprehensive screening.
- The Cogstate Brief Battery (CBB) is a cognitive screening assessment that has been described extensively within the literature, and has potential as a prescreening assessment tool. Cognitive impairment and progressive decline has been reported on the CBB in the context of preclinical and early AD.
- Several papers have been published on the utility of the CBB being administered in unsupervised or community contexts as an early indicator of cognitive impairment potentially associated with MCI or early AD.
- The aim of this study was to evaluate the CBB as a prescreening assessment to identify individuals with abnormal memory on the ISLT.

**Methods**

- Clinical sites identified subjects for potential entry into the elenbecestat studies who they believed would meet criteria for early AD (MMSE≥24; CDR 0–0.5; CDR Memory 0–0.5).
- Following consent, the ISLT immediate and delayed recall trials were administered, with the CBB being administered as a distractor between the ISLT immediate and delayed recall.
- The ISLT requires 5 minutes to complete and yields two performance measures: total words correct for immediate recall and delayed recall. The ISLT has been validated in over 90 countries, and new cultures and language groups are continually added to the library of available languages.

**Data Analysis**

- Logistic regression analyses were used to determine the optimal CBB equation to predict ISLT impairment. Each of the four tests in the CBB, as well as Age, were entered as independent variables into the logistic regression model. The dependent variable was ISLT impairment, defined as ≥1.00 on either the ISLT immediate or delayed recall.
- Once identified, the logistic equation was entered into a series of Receiver Operating Characteristic (ROC) analyses on the elenbecestat sample to determine correct classification rates of the CBB in predicting ISLT impairment.
- ROC analysis was then replicated on a combined sample of subjects in the elenbecestat studies (subjects impaired on the ISLT only) and normative controls (N = 4341, mean age = 70.99, SD = 4.69, range 64 to 86, 53.9% female).

**Results**

- The optimal CBB algorithm to predict ISLT impairment (immediate or delayed recall) for the elenbecestat sample included the Identification (attention), One Card Learning (visual learning) and One Back (working memory) tests. The final equation is provided below.

\[
\text{Pr [ISLT Impairment]} = 1 /[1 + e^{-[1.89 + [2.18 \times \text{Identification}] - [3.76 \times \text{One Card Learning}] - [1.86 \times \text{One Back}] + [0.03 \times \text{Age}] }]
\]

- Receiver Operating Characteristic (ROC) Analysis

- ROC analysis on the elenbecestat sample revealed an Area Under Curve (AUC) of 0.73 (95%CI 0.72, 0.74).
- Sensitivity of the model was 59.4%, whilst specificity was 21.2%.
- 77.1% of subjects were correctly classified by the CBB as impaired on the ISLT immediate or delayed recall, whilst 58.6% were correctly classified as not impaired.

**Figure 4. ROC curve for performance of impaired relative to unimpaired groups on the ISLT immediate and delayed recall tests for the CBB for impaired subjects from the elenbecestat sample (N = 5861) and a normative sample (N = 4341).**

**Conclusions**

- The optimal CBB logistic regression equation in predicting impairment on immediate or delayed recall of the ISLT incorporated two measures of memory (One Card Learning and One Back) and a measure of attention (Identification).
- Inspection of AUC statistics indicate high classification accuracy for the CBB in classifying impairment on the ISLT of immediate and delayed recall when this algorithm is applied.
- Findings suggest the CBB has potential as a prescreening tool for identifying impairment related to early AD.

**Disclosures**

Bruce Albala and Michelle Gee are full-time employees of Eisai Incorporated and Eisai Limited respectively. Paul Maruff and Adrian Scherber are full-time employees of Cogstate Incorporated.

**References**