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POSTER PRESENTATIONS
P2

P2-001 PRE-SCREENING PROCESS OF THE COLOMBIAN ALZHEIMER'S PREVENTION INITIATIVE TRIAL (API-COLOMBIA)

Margarita Giraldo[1], **Silvia Rios Romenets**[1], Hugo Lopez[1], Francisco Piedrahita[1], William Cho[2], Michael Ward[2], Pierre Tariot[3], Eric M. Reiman[3], Francisco Lopera[1], *[1]Neurosciences Group of Antioquia, University of Antioquia, Medellin, Colombia; [2]Genentech, Inc., South San Francisco, CA, USA; [3]Banner Alzheimer's Institute, Phoenix, AZ, USA. Contact e-mail: silvia.riosrom@hotmail.com*

Background: The Colombian Alzheimer's Prevention Initiative (API) Trial is a collaborative project involving the Neurosciences Group of Antioquia (GNA), Genentech/Roche, National Institute of Health, and the Banner Alzheimer's Institute, studying whether crenezumab can delay or prevent the clinical onset of Alzheimer's disease in asymptomatic carriers of the PSEN1 E280A mutation. With the goals of decreasing screen failures and optimizing participant compliance and adherence, GNA implemented a prescreening process. **Methods:** The prescreening process started with the generation of lists of probably eligible candidates between 30 and 60 years of age, who belong to the Colombian API Registry. Lists were created automatically by the SISNE2 system and filtered by the responsible analyst, who selected candidates in a 2:1 carrier/noncarrier ratio. The clinical history of each candidate was reviewed by a subinvestigator who evaluated health status and whether inclusion/exclusion (I/E) criteria were met. All eligible candidates were contacted by telephone and invited for group Informed Consent (IC) meetings in which the principal investigator explained the trial, possible adverse effects, and medical procedures performed at each visit. They were given the IC and the study brochure to review at home with their families. At the end of the meeting, candidates filled out prescreening questionnaires regarding current health status and confirming that I/E criteria were met. Candidates were contacted once by telephone to establish whether they wanted to participant in the trial. If they did, a screening visit was scheduled. Prescreening process was approved by a local Ethics Committee. **Results:** The total prescreening failure rate was 48.15%; of those, 66.6% were not invited to IC meeting due to not meeting specific I/E criteria. The most frequent causes for prescreening failures were: 39.0% expected inability to comply with visit, 13.0% mild cognitive impairment, 12.6% not in good health, 7.3% learning difficulties or illiteracy, 8.6% substance dependence, 6.6% pregnancy or willing to have kids and 6.0% dementia. **Conclusions:** The primary reason for prescreening failure in asymptomatic individuals was expected inability to comply with the visit schedule of the trial due to work related issues, which was anticipated since people are in a productive stage of their lives.

P2-002 EFFECT OF SOLANEZUMAB ON BIOMARKERS OF NEURODEGENERATION IN THE EXPEDITION3 TRIAL IN MILD ALZHEIMER DISEASE

Adam J. Schwarz[1], Karen L. Sundell[1], David Richard Lachno[2], Michael G. Case[1], Joyce Suhy[3], Michael J. Pontecorvo[4], Robert A. Dean[1], Eric R. Siemers[1], *[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Eli Lilly and Company, Windlesham, United Kingdom; [3]BioClinica, Inc., Newark, CA, USA; [4]Avid Radiopharmaceuticals, Philadelphia, PA, USA. Contact e-mail: schwarz_adam_james@lilly.com*

Background: Solanezumab is a humanized monoclonal antibody that preferentially binds soluble amyloid. Its efficacy in treating mild Alzheimer disease (AD), at an intravenous dose of 400mg administered every four weeks, was evaluated in a phase 3, double-blind trial in participants randomized to placebo (N=1072) or solanezumab (N=1057) (EXPEDITION3). Alongside clinical scales, volumetric magnetic resonance imaging (vMRI; in all patients) and cerebrospinal fluid (CSF; in a subset of patients) biomarkers reflecting neurodegenerative processes associated with AD were measured with the aim of assessing solanezumab's effects on longitudinal changes in these markers. **Methods:** 3DT1 scans for vMRI analysis (N=1043 (placebo) and N=1038 (solanezumab)), and CSF samples (N=188-208/arm, depending on the assay), were obtained at baseline and following 80 weeks of treatment. MRI scans were analyzed for hippocampal, entorhinal cortex, ventricular and whole brain volumes using Freesurfer-based methods. Total tau (*t*-tau) and phospho-tau 181 (p-tau$_{181}$) concentrations were determined from the CSF samples using validated INNOTEST(R) ELISA assays. An ANCOVA analysis of each biomarker compared the 80-week least square mean change in placebo and solanezumab groups. **Results:** The right hippocampal volume achieved a nominally statistically significant reduction in the rate of atrophy (p=0.032), corresponding approximately to a 6.7% slowing. Directionally, the other vMRI variables evidenced a reduced rate of atrophy in the solanezumab arm relative to the placebo arm, but these trends did not reach statistical significance ($0.077<p<0.32$). CSF *t*-tau increased by 98pg/mL in the placebo arm and by 173pg/mL in the solanezumab arm (p=0.06). CSF p-tau$_{181}$ increased by 4.96pg/mL in the placebo arm and by 6.98pg/mL in the solanezumab arm (p=0.56). **Conclusions:** In the EXPEDITION 3 study, solanezumab produced a consistent, but small, reduction in the rate of atrophy across different vMRI measures which achieved nominal statistical significance only for the right hippocampus. The small increases in CSF *t*-tau and p-tau$_{181}$ observed in both the solanezumab- and placebo-treated cohorts were not statistically significant.

P2-003 ELENBECESTAT PHARMACOKINETIC DRUG-DRUG INTERACTIONS INDICATED NO DOSAGE ADJUSTMENTS REQUIRED FOR MOST CONCOMITANT TREATMENTS

Bruce Albala[1], Robert YK. Lai[2], Jagadeesh Aluri[1], Peter Boyd[2], Min-Kun Chang[1], Satish Dayal[2], Jim Ferry[1], Bhaskar Rege[1], *[1]Eisai Inc., Woodcliff Lake, NJ, USA; [2]Eisai Ltd., Hatfield, United Kingdom. Contact e-mail: bruce_albala@eisai.com*

Background: Elenbecestat (E2609) is a BACE inhibitor primarily metabolized by carboxylesterase 2 (CES2) and to lesser extent by CYP3A. Drug-drug interaction studies assessed the effects of itraconazole (strong CYP3A and CES2 inhibitor), rifampin (strong CYP3A inducer), and donepezil on elenbecestat pharmacokinetics, as well as the effects of elenbecestat on digoxin (Pgp substrate) pharmacokinetics. **Methods:** This open label study in healthy adult subjects was conducted in 3 parts. Part A: subjects received a single oral dose of elenbecestat 50 mg on day 1; from day 6 to 20, subjects received daily doses of either itraconazole 200 mg or rifampin 600 mg; with a second dose of elenbecestat 50 mg on day 14. Part B: subjects received digoxin 0.25 mg on day 1, elenbecestat 50 mg/day from day 7 to 20, and a second digoxin dose at day 14. Part C: a 3-way crossover study in which each subject received a single dose of elenbecestat 50 mg, elenbecestat 50 mg in combination with donepezil 10 mg, and