



## Corrigendum

## Corrigendum to “17th Clinical Trials on Alzheimer’s Disease (CTAD) Madrid, Spain, October 29 - November 1, 2024: Symposia, Oral Communications” [J Prev Alzheimers Dis 2025;12(1S):100043].



Below an abstract which is missing in the publication of the referenced CTAD supplement.

The editors and the publisher sincerely apologize to the authors of the abstract and to the readers of the journal for this mistake.

### OC10 PROSPECT-ALZ: Results of the phase 2 study of ceperognastat, an orally available O-linked N-acetyl glucosaminidase inhibitor for the treatment of early symptomatic Alzheimer’s disease

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**Background:** O-linked N-acetyl glucosaminidase (OGA) is a glycoside hydrolase enzyme that catalyzes the removal of a sugar residue, O-linked  $\beta$ -N-acetyl glucosamine (O-GlcNAc), from intracellular proteins such as the microtubule-associated protein tau. OGA inhibition increases the presence of O-GlcNAc on tau protein and, in animal models of tauopathy, has been shown to slow the accumulation of hyperphosphorylated, insoluble tau, including neurofibrillary tangles.<sup>1,2,3</sup>

**Methods:** PROSPECT-ALZ (NCT05063539), a multicenter, double-blind, randomized placebo-controlled phase 2 study of ceperognastat, an orally available OGA inhibitor, enrolled participants with early symptomatic Alzheimer’s disease (AD). Participants (n=327) aged 60-85 years, had elevated plasma P-tau217 (where available), and a tau PET (18F-flortaucipir) scan demonstrating the presence of tau pathology by visual and quantitative assessment. Participants were randomized 1:1:1 into three arms: 0.75 mg or 3.0 mg ceperognastat, or placebo, given once daily. PROSPECT-ALZ utilized a common close design with a dosing duration ranging from 76 to 124 weeks. The primary objective was to evaluate the effects of ceperognastat on clinical progression in participants with low-medium tau PET levels at baseline (primary cohort), measured by the integrated AD Rating Scale (iADRS) using a Bayesian Disease Progression model, where a disease progression ratio (DPR) of <1 favors treatment compared to placebo. Secondary endpoints, in both the low-medium tau and full-study population, included additional cognitive and functional scales and biomarkers of AD.

**Results:** Baseline demographics and clinical characteristics were balanced across cohorts. The mean of the posterior distribution of the DPR comparing 0.75 mg or 3.0 mg ceperognastat to placebo on iADRS in the primary cohort was 0.84 (95% CrI: 0.66, 1.04) and 1.32 (95% CrI: 1.10, 1.58), respectively. In the full-study population, DPR was 0.87 (95% CrI: 0.72, 1.04) and 1.43 (95% CrI: 1.22, 1.65), respectively. Other secondary clinical assessments failed to show significant dose-dependent benefit of ceperognastat versus placebo. Secondary biomarker assessments at 76 weeks, included volumetric MRI which showed less decrease in whole brain and hippocampal volume, and less increase in ventricular volume in both treatment arms compared to placebo. Depending on the region, Tau PET demonstrated less increase from baseline at 76 weeks in the primary cohort with 3 mg. Plasma P-tau217 showed less increase from baseline at multiple timepoints in both treatment arms. Additional biomarker data will be presented. Common adverse events in the treatment arms included headache, cardiac-related events, and weight decrease. A higher frequency of serious adverse events in the nervous system, psychiatric and cardiac disorders were reported in the 3 mg ceperognastat arm. Two deaths (pneumonia and encephalitis) were reported during the study, with a third adverse-event-related death (hematological malignancy) occurring 17 days after discontinuing from the study. All three deaths were reported as unrelated to study treatment. A post-treatment safety extension is ongoing.

**Conclusions:** PROSPECT-ALZ did not demonstrate that ceperognastat slows clinical disease progression in early symptomatic AD and worsened progression at 3 mg. Ceperognastat was associated with less brain volume loss and reduction in tau accumulation versus placebo. A higher incidence of certain adverse events was observed with ceperognastat compared to placebo.

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**Keywords:**

Ceperognastat, anti-tau therapy, Oglcnacase, tau, neurofibrillary tangles

**Disclosures:** Adam S. Fleisher, Leanne Munsie, Michele Mancini, Eden Yun-Ju Cheng, Sergey Shcherbinin, Tomomi Nakamura, William Kielbasa, Hugh Nuthall, Dustin Mergott, Mark Mintun, and Mirosław Brys are employees and minor shareholders of Eli Lilly and Company.