FC16: Timing and Duration of Adverse Events During Treatment of Agitation in Alzheimer's Dementia with Brexpiprazole: Pooled Results From Three Phase 3 Trials

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Objectives: Antipsychotic use among patients with Alzheimer's dementia can pose safety concerns, including accidents/injuries, cardiovascular events, extrapyramidal symptoms, and somnolence/sedation. In the US, brexpiprazole is approved for the treatment of agitation associated with dementia due to Alzheimer's disease. This post hoc analysis aimed to evaluate the timing and duration of treatment-emergent adverse events (TEAEs) in three randomized clinical trials of brexpiprazole.

Methods: Data were included from three Phase 3, 12-week, randomized, double-blind, placebo-controlled trials of brexpiprazole in patients with agitation associated with Alzheimer's dementia (ClinicalTrials.gov identifiers: NCT01862640, NCT01922258, NCT03548584). Data for all patients who received ≥1 dose of trial medication were pooled by randomized dose group: brexpiprazole 0.5 or 1 mg/day (fixed-dose), brexpiprazole 2 or 3 mg/day (fixed-dose) (FDA- approved recommended-to-maximum dose), brexpiprazole 0.5 – 2 mg/day (flexible-dose), and placebo. Time-to-event analyses were performed to first occurrence of any TEAE, any serious TEAE, discontinuation due to AE, and TEAEs of interest, separately, and presented using descriptive statistics and Kaplan–Meier Methodsology. The duration of all TEAEs in each category was also determined.

Results: The pooled sample comprised 1,043 patients. Median time to first TEAE was 24 days with brexpiprazole 0.5 or 1 mg/day (fixed-dose), 32 days with brexpiprazole 2 or 3 mg/day (fixed-dose), 28 days with brexpiprazole 0.5–2 mg/day (flexible-dose), and 28 days with placebo. Median duration of all TEAEs was 7 days, 6 days, 8 days, and 4 days (respectively). Median time to (and incidence of) discontinuation due to AEs was 45 days (8.9%) with brexpiprazole 0.5 or 1 mg/day, 46.5 days (4.9%) with brexpiprazole 2 or 3 mg/day, 30 days (6.8%) with brexpiprazole 0.5 –2 mg/day, and 30 days (3.4%) with placebo. The incidence of serious TEAEs and TEAEs of interest is presented in the Table.

Conclusions: In patients with agitation in Alzheimer's dementia, time to first occurrence of any TEAE was similar between brexpiprazole 2 or 3 mg/day (FDA-approved recommended-to- maximum dose) and placebo, and time to discontinuation due to AEs was longer with brexpiprazole 2 or 3 mg/day than placebo. Overall, no unexpected safety concerns were revealed by this analysis.

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