Protocol Title: Treatment of Psychosis and Agitation in Alzheimer's disease

Document Title: Statistical Analysis Plan

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Statistical Analysis Plan

A detailed description of the statistical analysis plan was published (25). Analyses were based on the Intent-To-Treat (ITT) principle, including every patient who was randomized. All tests were performed at two-tailed significance $\alpha=0.05$.

To test the primary hypothesis, i.e., lithium will significantly reduce agitation/aggression compared to placebo, a linear mixed effects model (MEM) was used with visit (baseline versus 12 weeks), group (placebo versus lithium) and their interactions as fixed effects and a random intercept per patient to account for within-subject correlation due to repeated measurements. Differences in the least squares means (treatment effects) in each group with 95% confidence intervals were derived. For the secondary hypothesis and related categorical outcomes, χ^2 test or Fisher's exact test was used. For other secondary and exploratory efficacy outcomes, MEM was used for continuous outcomes as appropriate, including change in TESS scores and other adverse effect outcomes. Standardized effect sizes using Cohen's d for continuous outcomes (33) and odds ratios for categorical outcomes are reported.
We used the RMASS program for power analysis for longitudinal studies. For the originally projected sample size of 80 patients, under moderate or weak within-subject correlation we estimated 80% power to detect a medium to large effect size of d=0.5 if dropout was 15% and correlation was 0.36. The actual sample size was 77 patients with 24.7% dropout, thereby lowering statistical power.