Optimizing Binge Eating Disorder Drug Development using a Quantitative Disease-Drug-Trial Model

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Background and Objectives: The development of drugs to treat binge eating disorder is challenged by high dropout rates due to lack of efficacy and long follow up times. The objective of this analysis is to inform future BED clinical trials using a quantitative disease-drug-trial framework that takes into account longitudinal placebo and drug effects on primary and secondary efficacy variables and dropout rates.

Methods: Longitudinal normalized binge frequency (BF) from a double blind, randomized placebo controlled, titration trial (N=61) that evaluated the use of topiramate for BED, was used to develop the disease-drug trial model [1]. Model building consisted of (1) developing a placebo effect model that describes longitudinal data from the placebo group, (2) adding a dose effect to the placebo model to evaluate the impact of varying treatment doses on BF, (3) using a kinetic-pharmacodynamic (K-PD) model to justify the delay in changes in BF, and (4) creating a parametric time to event model to characterize patient dropout patterns. Secondary efficacy variables (modified Yale-Brown Obsessive/Compulsive Scale, global severity of illness score, and change in weight) were predicted based on individual predicted BF scores.

Results: The placebo effect on normalized BF over time demonstrated a maximum decrease in BF of 50% by 4 weeks. Baseline global severity of illness scores was found to be a significant covariate on baseline BF. The K-PD model adequately explained the delayed effect on changes in BF with a time to reach maximum decrease in BF of 80% by 7.5 weeks. Patients were found to have a higher drop-out probability if they gained or maintained their weight during the trial.

Conclusion: The developed comprehensive disease-drug-trial model linking primary and secondary efficacy variables will be used to simulate different clinical trial designs to optimize topiramate and similar BED drug development programs.