Advancement of a Drug-Disease-Trial Model for Alzheimer’s Disease Through a Regulatory Science Path: The CAMD Experience

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Critical Resources

Knowledge Integration

Applications

Previous modeling and simulation contributions Panel A (like the use of a Bateman function to describe the placebo effect) were incorporated with new contributions Panel B (like the use of beta-distributed residuals so the predicted ADAS-cog scores are bound within 0-70).

The develop model encompasses the following components:
- Natural progression of disease
- Placebo effect
- Symptomatic and disease-modifying drug effects
- Drop-out model

Simulations based on the model can help design teams tackle different questions, like the selection of a specific design given a particular drug effect (the example in panel A shows a disease-modifying drug in the context of a standard parallel design and in a delayed start design), or the time-varying probability of dropouts given trial entry criteria (panel B).

Regulatory Pathway

The successful development of the current AD drug disease-trial model was made possible by the consortium approach—a large network of stakeholders that partnered to share expertise, costs, and risks—and was accelerated by continuous regulatory engagement. The quantitative disease model will be made publicly available.

CAMD is based on sharing non-competitive patient level data from legacy clinical trials, and leveraging applicable knowledge for Alzheimer’s and Parkinson’s diseases. A coalition of multiple stakeholders developed an analysis plan for a drug-disease-trial model in mild and moderate AD patients with the ADAS-Cog cognition measure as the primary outcome, using a 6000+ patient standardized database, ADNI and the available literature.