Progression Prediction Algorithms Poised to Speed Clinical Trials

By Richard Robinson

Big data is coming to ALS clinical trials and its arrival is likely to make them faster and more informative, speeding the testing of new therapies. The potential of large amounts of data to shape ALS trials was outlined in a recent webinar by Origent, Inc. Chief Scientific Officer David Ennist, Ph.D., M.B.A.

Origent is an outgrowth of Sentrana, a marketing analysis firm, which uses detailed information about customer behavior to make predictions about future purchases. That same idea—that by accumulating the right information, one can make an accurate prediction about the future—is the basis of Origent’s prediction algorithms (i.e. a formula to solve a problem). Sentrana was one of two winners of the ALS Progression Prediction Challenge, sponsored by Prize4Life. Liuxia Wang, Ph.D., the scientist who won the prize, is Origent’s principle scientist and chief modeling expert.

“We use machine learning techniques to develop patient-level predictive models,” Dr. Ennist explained. “We ingest data, run it through our models and make individual predictions for each patient” within a database. Those predictions are then tested against actual outcomes and the successes and failures in the predictions are then used to make the algorithm model smarter for the next round.

For the Prize4Life Challenge, the team digested clinical data of more than 1000 people with ALS who had enrolled in large clinical trials. They sought to determine which clinical data—such as age of onset, baseline respiratory function, levels of substances in the blood, etc.—collected during the first three months of the trials would best predict survival or other outcomes one year later. By choosing subsets of the data and tweaking their relative importance in many thousands of simulations, they arrived at a set of highly predictive algorithms for survival, such as the ALS Functional Rating Scale (ALSFRS) score, respiratory function and other important clinical variables. For example, Dr. Ennist stated, “The ALSFRS (algorithm) model does a very good job of predicting the ALSFRS score a year into the future.”

The algorithms are not meant for an individual person with ALS in the clinic to use, at least not yet. Instead, Dr. Ennist envisions they will be used by pharmaceutical companies to shape clinical trials, especially in the early stages of drug testing.

“They can be used to stratify patients at the beginning of a trial,” he said, for instance into subgroups of fast and slow progressors. That way, the effect of a drug on progression could
more easily seen, because the background rate of progression in each subgroup would be much more similar.

The algorithms could also be used, in some cases, to replace a control group. A control group is used as a comparison, for example, to understand how progression differs between those who receive treatment and those who do not. The algorithms may allow an individual’s progression to be predicted at the start of the trial and their actual progression could be compared to that prediction at the end of the trial.

A similar kind of analysis could be used to determine which people receiving treatment may have responded to it, allowing them to be analyzed separately for clues as to what distinguishes responders from non-responders. That information can then be used to design better treatment or to shape future clinical trials.

The ability to better predict likely progression can also make trials smaller and faster. If during the trial researchers have a better understanding of what they should expect to see and when, they can end the trial sooner if they do not see the predicted outcomes. This would end unproductive trials more quickly, allowing other more effective trials to start, thereby accelerating the search for an effective treatment.

The ALS Association provided funds to Origent to expand the data set they use for developing their algorithm models, which should make them even more accurate. As new biomarkers become validated, they will also be worked into the models. The company is currently working with the Food and Drug Administration (FDA) to receive approval for the algorithms for use in clinical trials. Dr. Ennist hopes to see that next step taken within three years.

“We are very excited to see this tool develop,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., M.B.A. “Use of data in this way has the potential to accelerate clinical trials and to teach us important things about ALS at the same time.”