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PharmaVOICE

The Clinical Trials Technology Ecosystem

Technology improvements are enhancing R&D efficiency, accelerating time to market, improving safety, and boosting data accuracy — all of which are increasing the success rates for pharmaceutical sponsors and their clinical trial partners.

Determining Dosing for Specialty Populations

Roche's Tamiflu, an antiviral drug that can make flu symptoms milder and can shorten the duration of illness, had unique design and dosing challenges. Tamiflu was first approved in 1999 for adults and then later for children older than 12 months of age. But determining the dosing for the antiviral for children under 12 months of age was a special challenge for the company.

Scientists at Roche and the National Institutes of Health had to design studies and dosing regimens for Tamiflu for different age infants. The challenge was how to integrate, analyze, and present the data from these data-intensive studies in a way that would enable regulators to make a decision about infant dosing.

A critical part of the submission strategy was the development of mathematical models to analyze the pharmacokinetic and pharmacodynamic data and the incorporation of this information throughout the clinical pharmacology package submitted to the FDA to support infant dosing.

A modeling approach by pooling data from several trials is a great way to integrate prior knowledge. This way, we increase the power of statistical analysis.

DR. BRUNO REIGNER
Roche

"We wanted to integrate knowledge coming from different trials," says Bruno Reigner, Pharm.D., Ph.D., head clinical pharmacology — established products, Roche Pharma Research & Early Development. "With this model, we could analyze all the raw data coming from the different clinical studies and create a small meta-analysis. By doing this, we increased the power of the analytics."

Based on the results from this model-based analysis, Roche received approval for dosing in infants as young as 2 weeks old in 2012.

"These processes supporting the filing with the FDA took about six months," says Craig Rayner, Pharm.D., president of d3 Medicine, a Certara company that lead the clinical pharmacology program.

"Without the clinical pharmacology strategy incorporating the modeling activities, there likely would not have been labeling for an infant dose. If we had looked at the data in the traditional ways using a noncompartmental analysis of different data sets, it would have been very difficult to make the case because the data were so heterogeneous. Without the power of pooling and binding the evidence in a way that is defendable and scientifically credible, a likely outcome would have been the physician community being left to make decisions about dosing in infants on the basis of publications from clinical trials with important design differences."

Dr. Reigner says without this modeling, Roche may have needed to do additional or larger studies in infants.

"Pediatric trials are very difficult to conduct, especially those with children younger than 1 years old," he says.

The burgeoning information content and the availability of modeling tools means that the pharma industry has to continue to evolve its development mindset to consider the stakeholders: payers, regulators, and patients.

DR. CRAIG RAYNER
d3 Medicine, a Certara company