PK/PD, BIOMARKER + MODEL-BASED DRUG DEVELOPMENT: WHERE TO START?

Dr. Ulrich Roth

Drug Metabolism and Pharmacokinetics, Boehringer Ingelheim Pharma GmbH & Co. KG, Birkendorfer Strasse 65, 88397 Biberach / Riss, GERMANY

Abstract body

DMPK since many years has expanded from pure ADME into the fields of PK/PD. In more recent years, while gaps in both, productivity and innovation, rising regulatory hurdles, cost pressure in health care, etc. make drug development riskier and more expensive, pharmaceutical companies seek new ways to identify those candidates with higher probability of success early, i.e. before investing in costly large-scale clinical trials.

Using biomarkers, pharmacogenetics and advanced modelling + simulation techniques (“model-based drug development”) are state of the art, so called “translational” approaches to achieve this goal. Therefore “PK/PD as a functional linkage between drug discovery and development” calls for the systematic (structured and organized) integration of many different disciplines to closely collaborate. The goal is to create knowledge on the drug candidate’s (or the compound class) pharmacokinetics and –dynamics that not only serves regulatory purposes, but aids our understanding of physiological targets, disease mechanisms, compound characteristics, and molecular mechanisms of drug effects and help identifying patient populations most responsive to a new drug. This knowledge is important as the basis for internal decision making to find the best way forward during lengthy and costly drug development.

At Boehringer Ingelheim we have introduced dedicated functions for biomarkers, pharmacogenomics (including DNA-banking), and pharmacometrics (modelling + simulations) next to the well established classical, therapeutic area based functions in the Drug Discovery and Medical organizations. Most recently we began to evaluate the potential use of mass spec technologies in the field of biomarkers at BI’s Pharma Research Institute in Kobe closely collaborating with Japanese academia.

Looking at the value chain of the drug discovery and development process, the question is not only, which disciplines are needed, but also what they should contribute at which point in time and how this should be organized? In three pilot projects we are currently collecting valuable real-life experience to identify the key success factors, which can then be implemented in the organization across projects. The following have been already identified: 1) to start early, i.e. already during drug discovery phases, 2) to foster close interaction and collaboration using a project team setting and applying a milestone concept with defined deliverables, 3) to assign clear tasks and responsibilities which are complementary to each other for the following key areas: (nonclinical) DMPK, pharmacology, biomarkers, pharmacogenetics, pharmacometrics, clinical PK, toxicology, medical experts in respective therapeutic areas, and medical experts with background in translational approaches as well as in the clinical trial conduct employing biomarkers. 4) to build a network among key functions that amplifies and carries knowledge continuously within and across the therapeutic areas and projects from preclinics to the clinics (and back to the bench).

Biography

- Chemist
- PhD in Biochemistry
- Head of Laboratory, Clinical PK, Boehringer Ingelheim / Germany
- R+D Project Leader, Boehringer Ingelheim / Germany
- Director, DMPK, Boehringer Ingelheim / Ridgefield, USA
- Vice President, DMPK, Boehringer Ingelheim / Biberach, Germany