Conference abstract L13

Translational Medicine: Pharmacokinetic and Pharmacogenetic Aspects of Personalized Pharmacotherapy

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Variability among individuals that affects clinical outcome is still one of the major challenges in drug development and in the practice of medicine. No single drug is 100% efficacious in all patients. While some individuals obtain the desired effects, there can be no or little therapeutic response in others. Additionally, some patients might experience adverse effects. This interindividual variability is a consequence of myriad of factors, such as disease states, genetic factors, patient age, concomitant medications, and life style factors such as smoking. Most drugs undergo biotransformation and their disposition in the body may involve multiple transport proteins. In addition, they interact with diverse protein targets. This concerted action results in the multigenic nature of a majority of drug responses. Pharmacogenomics, in the future, may provide a complex and more precise set of tools for clinicians to use for diagnosis and treatment. Extensive pharmacometric expertise and model building enables personalization of therapies, which is far from trivial if one considers the complexities of designing the most effective dosage regimen of one or more drugs in conjunction with novel biomarkers. Population pharmacokinetic/ pharmacodynamic methods, such as nonlinear mixed effects modeling are able to obtain relevant information in patients who are representative of the target population. They recognize sources of variability such as inter- and intraindividual as important drug characteristics, and seek to explain variability by identifying various covariates, including genetic factors. Additionally, they aim to quantitatively estimate the magnitude of the unexplained part of the variability, which is important because the efficacy and safety of a drug may decrease as unexplained variability increases. This presentation will demonstrate how pharmacogenetics and population pharmacokinetics can personalize treatment with warfarin, leflunomide [1], and risperidone [2].

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