Advances in translation of preclinical pharmacology and toxicology to the clinic

○ Kay A. CRISWELL

Drug Safety Research and Development, Pfizer Inc., USA

Translating nonclinical data and observations into possible clinical outcomes can make the drug development process more efficient and cost-effective. Additionally, translation allows a better understanding of drug toxicities and human relevance, which aligns with the heightened regulatory emphasis on the delivery of safer medicines with fewer side effects. Despite enhanced efforts to understand and derisk targets for potential safety issues, cardiovascular toxicity, hepatotoxicity, and nephrotoxicity continue to halt clinical trial progression and contribute to post-marketing withdrawals of new medicines. Even areas of expected high translation from preclinical to clinical outcomes such as hematotoxicity continue to cause > 10 % clinical attrition. This presentation will focus on translatability of biomarkers and models in these four high areas of attrition and highlight new models and assays that may enhance translation. Safety risks associated with other target organs occur less frequently, but also remain problematic in drug development. A few examples of exploratory preclinical models in areas that demonstrate known gaps in translation, such as testes toxicology, will also be covered. Translation of preclinical toxicology findings remains pivotal in drug development. It allows us to answer two key questions surrounding the relevance of preclinical results: (1) How can we guard against drug-induced injuries seen in the clinical but not in preclinical toxicology and (2) How can we continue to advance development of good drugs that show toxicity in animals that are not expected to be present or relevant in humans?