The successful approach of The Critical Path Institute’s Predictive Safety Testing Consortium public-private partnership in qualifying biomarkers for drug induced kidney injury

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The ability of biomarkers to improve treatment and reduce healthcare costs is potentially greater than in any other area of current medical research. However, understanding the characteristics of novel biomarkers and developing the robust evidentiary packages to support incorporating them into drug development and clinical practice is an enormous undertaking requiring significant resources and commitment from a wide range of stakeholders, including regulatory, industry and academic scientists. The Predictive Safety Testing Consortium is a unique public-private partnership formed by the Critical Path Institute to identify new and improved safety testing methods and submit them for formal regulatory qualification by the Food and Drug Administration (FDA), European Medicines Agency (EMA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). Nephrotoxicity is a serious problem for drug development and the sensitivity and specificity of accessible biomarkers of nephrotoxicity in current use (particularly BUN and serum creatinine) does not allow early detection of drug-induced kidney toxicity. This results in significant risk to patients and the termination of drug development for potentially innovative compounds for unmet medical needs because of the inability to monitor for early toxicity. In 2008, the PSTC obtained the first qualification of seven urinary renal preclinical safety biomarkers for use in rodent studies, and on a case-by case basis for the inclusion into clinical development. These included KIM-1, clusterin, TFF-3, albumin, β2-microglobulin, total protein and Cystatin C. The PSTC has continued to expand this qualification by increasing the number of biomarkers, assessing prodromal and reversibility characteristics and regional specificity for these biomarkers. In addition, these biomarkers are being examined in canine and primate models. Furthermore, the PSTC is collaborating with the FNIH Biomarkers Consortium on a large clinical program to define thresholds and characterize the performance of these new biomarkers in humans in order to enhance decision making in drug development, particularly for drug candidates that exhibit nephrotoxicity. This session will focus on the success of the preclinical renal safety biomarker qualification, the impact this qualification is making on drug development and the translational activities for the progressive qualification of novel renal safety biomarkers which are needed today.