Drug-induced kidney injury (DIKI) is not an uncommon adverse event in drug development. The challenge being late identification of acute kidney injury due to the current standards (i.e. serum creatinine (sCr) and blood urea nitrogen (BUN)) which may not be significantly changed until 2/3 of the kidney function has already been lost. Over the last three years, we have seen great progress with preclinical qualification processes for kidney biomarkers. The PTCI and I3H EHE have both had rat kidney biomarkers qualified by both the FDA and EMA. These landmark qualifications mean that drug companies may now use certain novel preclinical markers for real decision making within their drug discovery process.

**Biomarkers Selected**

SAFE-T are using commercially available assays for the candidate biomarkers selected where available. Through a series of low and high bar validation processes the markers have been screened for their suitability for entry into the clinical sample assessment. SAFE-T selected the above biomarkers through a comprehensive analysis of over 50 candidates. These markers were assessed for factors such as; published clinical data, published preclinical data, availability of assay, stability, assay and analyte kinetics and stability, IP suitability, etc. From this list of 50, 21 biomarkers were chosen for assessment. For some of the markers that are available on multiple technologies (EUSA, Luminex, Mesoscale, etc.) the consortium has undertaken dual technology assessment.

**Stage Gate Analysis**

To optimize the assessment of these biomarkers it was decided to investigate a subset of the exploratory studies to enable SAFE-T to drop markers with high variability in healthy volunteers and no or minimal responses to drug induced kidney injury (according to established criteria, i.e. AKIN, KDIGO, RIFLE). A clinical adjudication committee was established and investigated each patient’s clinical data to identify AKI patients and exclude patients with protocol failure or too few samples / data collected.

**Next Steps**

- Complete the assessment of the candidate biomarkers with the stage gate cohort of samples
- Select the leading candidates to proceed to the confirmatory clinical studies and drop those that are too variable in a healthy cohort or too insensitive with clear AKI cases as identified by adjudication committee.
- Analyze the selected biomarkers in the entire population of the exploratory clinical studies
- Seek regulatory advice and approval (with the FDA and EMA) for the proposed confirmatory study(ies)
- Plan prospective confirmatory trials. Currently two trials for the confirmatory phase are anticipated
- Prepare a qualification submission to the regulatory authorities with the leading biomarker(s) that demonstrate value in identification of drug induced kidney injury and have clinical utility.