BmDR
BIOMARKER DATA REPOSITORY
CRITICAL PATH INSTITUTE

Advancing Drug Development. Improving Lives. Together.

Dear DIKI Biomarker Workshop Participants & BmDR Enthusiasts,

Thank you for your continued interest, participation, and contributions to the Biomarker Data Repository. The Oversight Committee has been busy refining our processes and connecting with research and patient groups involved in kidney disease. We plan to make this newsletter a quarterly publication moving forward. This quarter we have updates on progress towards this year's goals; physicians' perspective on the need for the repository and corresponding research; an update from the BmDR Oversight Committee's Co-Chairs; and conclude with an overview by the nephrologists who provided blinded, expert adjudication of the clinical studies supporting qualification of the emerging kidney safety biomarkers and the approach taken to adjudicate drug-induced kidney injury.

Sincerely,

Nicholas King
Executive Director,
Predictive Safety Testing Consortium

Latest Developments

This year the BmDR team is focusing on expanding the volume and capabilities of the repository. First, we are reaching out to consortia, academic researchers, and companies with relevant data sets to contribute. Second, we are attending meetings and conferences to spread the word about BmDR and elicit data contributions. We are currently building a data and analytics platform (DAP) for review and interrogation of the data. If you'd like to see an example of another C-Path DAP, please visit this link: **https://portal.rdca.c-path.org**. The BmDR DAP is estimated to be ready for public access by July 2024; once deployed, we will provide access instructions.

The BmDR Oversight Committee is busy working in sub-committees focused on communications and publications, community engagement, and legal and technical components of the BmDR. We are finalizing our communication and publication strategy for the next year, with these newsletters being one component of the communication strategy. We are currently preparing four submission applications for poster presentations at this year's American Society of Nephrology's (ASN's) Kidney Week. High level topics listed below:

1. Value of the BmDR
2. Data Sharing and Establishing a Core Set of Case Report Forms (CRFs)
3. Nuances of Adjudication
4. DAP User Interface

The BmDR legal sub-committee is updating components of the data contribution and use agreements, while the technical sub-committee is determining the appropriate clinical study data sets to obtain to support the initial focus of the BmDR on drug-induced kidney injury.

Physicians' Voices

Dr. Stefan Sultana (AstraZeneca): Having a panel of qualified safety biomarkers for use in Phase 1 healthy volunteer studies has made a big difference to the way that new molecules with the potential to cause kidney injury can be tested in a safe and controlled manner. Using these biomarkers to show that these new molecules are safe in healthy individuals allows us to progress and test them in patient studies. These biomarkers are also being assessed for use in patient studies. Currently, the biomarkers are used on a case-by-case basis but, once qualified, the biomarker panel can be used more widely and consistently, thereby improving kidney safety monitoring in patients in clinical trials and beyond.

The biomarker data repository will enable pharmaceutical companies, academic groups, diagnostic test manufacturers and other interested parties to pool existing data. This will speed up efforts to discover new biomarkers or new uses for existing biomarkers to monitor for different types of kidney injury. Kidney safety research has never been more exciting!

Co-Chair Corner

Biomarker Data Repository (BmDR): A Call to Action

"We need your help! As a patient and a practicing nephrologist, respectively, we can assure you that chronic kidney disease (CKD) and acute kidney injury (AKI) pose significant challenges to patients and healthcare systems worldwide. The timely identification of novel biomarkers related to AKI and CKD holds immense importance for improving research, advancing patient care, and improving outcomes for people living with kidney diseases.

The BmDR is not merely a quest to identify novel kidney disease biomarkers for scientific curiosity. It will directly impact patients' lives. Biomarkers serve as endpoints in clinical trials, facilitating drug development. The identification of new biomarkers will enable researchers to evaluate treatment efficacy and safety more accurately.

The quest to identify novel and innovative biomarkers holds the promise of early detection, improved prognosis, and better patient care. By identifying and validating new markers, we will empower patients with the information they need to enable and support lifestyle choices. Also, identifying and validating new markers will provide clinicians with the data and tools to advance the standard of care by tailoring treatments and facilitating personalized medicine for each patient.

This pre-competitive, collaborative effort will benefit all interested parties. It is not about surrendering competitive advantage; rather, it is about amplifying collective progress and making life better for all of us. By contributing to the BmDR we can better navigate uncertainty and shape a better future together. If you help us, we all win.

Join us. Contribute your data to the BmDR.

~Glenda V. Roberts & Gary Friedman

If you are interested in participating in the BmDR Oversight Committee or one of the sub-committees, please contact Nick King (nking@c-path.org) or Katrina Peron (kperon@c-path.org).

Adjudicator's Corner

Adjudication is the process of wherein trained healthcare practitioners (physicians and non-physicians) evaluate serial biomarkers data (standard and novel biomarkers) over time to discern presence and or absence of clinical acute kidney injury (AKI) as well as the presence or absence of sub-clinical injury. This is useful in the pursuit of:

- **Regulatory Agency full qualification of novel biomarkers:** it is necessary to demonstrate the degree to which panels of expert physicians independently evaluate blinded, time-sequenced biomarkers data to make timely clinical decisions in sufficient numbers of study participants.
- **Academic clinical and research objectives:** decision-makers (physicians and non-physicians) achieve consensus by individually or cooperatively reviewing time-sequenced biomarkers data to determine the presence or absence of kidney injury, time to injury resolution, and inform patient response to treatment longitudinally.
- **Pharmaceutical drug development:** physician and non-physician clinical drug development experts evaluate time-sequenced biomarkers data to assess Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) drug safety in active and placebo treatment groups.
- Optimization of AKI and chronic kidney disease (CKD) management in patient care.

Standard biomarkers (serum creatinine, serum cystatin C, estimated glomerular filtration rate (GFR), Urine Albumin or Protein to Creatinine Ratio [UACR and UPCR]) used in conjunction with qualified and non-qualified novel biomarkers have the potential to advance the evolution of acute and chronic disease diagnostics, as well as treatment response prognostication. It is the intent of the "BmDR Adjudication Corner" to periodically assess high quality data from the above pursuits to provide patients and caregivers, healthcare professionals, and industry researchers common awareness of the evolving utility of combined standard and novel biomarkers and (when appropriate) provide evidence supporting novel contexts of use for contemporaneous novel and standard biomarkers.

Healthcare professionals (HCPs) and Pharma Clinicians have experience adjudicating the PSTC biomarkers for regulatory approvals and for clinical safety in trial cohorts, respectively:

Steven Coca (Professor, Icahn School of Medicine, Mt. Sinai School of Medicine): "The variety of patterns in elevation of the panel of novel biomarkers of kidney tubule injury that we observed during the adjudication process was remarkable. Most of the injury patterns occurred without clear evidence of AKI by the current clinical standard of changes in filtration markers. We are eager to understand the clinical significance and implications for the field are for the 'subclinical acute tubule injury'."

Jai Radhakrishnan MD (Clinical Chief, Nephrology Division, NY Presbyterian Medical Center): "In my experience as an adjudicator, I found the BmDR Adjudication Corner as a potentially pivotal source for evaluating high-quality data on standard and novel biomarkers. By providing a comprehensive analysis, this program could tremendously help in designing clinical trials focused on medications with potential kidney toxicity. Although the (meticulous) adjudication of data required considerable effort, I realized that if successful we could potentially identify novel contexts of use to enrich clinical decision-making and perhaps pave the way for a 'personalized medicine' approach."

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FDA Acknowledgment