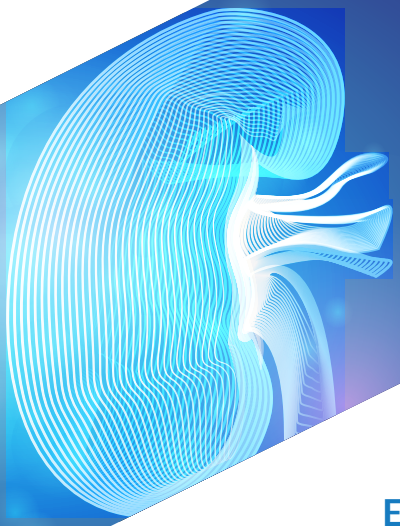
PKD
POLYCYSTIC KIDNEY DISEASE OUTCOMES CONSORTIUM



POLYCYSTIC KIDNEY DISEASE OUTCOMES CONSORTIUM (PKDOC) 2020

Executive Summary

The Polycystic Kidney Disease Outcomes Consortium (PKDOC) is a successful collaboration between Critical Path Institute (C-Path), the PKD Foundation, leading academic medical centers, pharmaceutical companies, patient organizations, and international regulatory agencies including the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and Health Canada (https://c-path.org/programs/pkd/). Its mission is to develop tools and promote research that will support the development and regulatory approval of new treatments for PKD and improve the lives of all it affects. The primary accomplishment of the consortium to date is the successful qualification of Total Kidney Volume (TKV) as a prognostic biomarker with both the US FDA and the EMA (European Medicines Agency, 2015; U.S. Food and Drug Administration, 2018). In 2018, the FDA designated TKV as a reasonably likely surrogate endpoint (U.S. Food and Drug Administration, 2020), an impactful step forward to support PKD drug development.

The PKDOC team includes leadership representation from a C-Path Executive Director and Co-directors from the PKD Foundation, industry and academia. C-Path staff also provide project management and administrative support. Currently, the PKDOC team hosts monthly meetings to assess the challenges in PKD drug development, determine potential solutions to overcome these challenges, and align and implement these solutions across stakeholders. Anyone who is interested may participate. To join PKDOC please contact John-Michael Sauer, Executive Director (PKDOCInfo@c-path.org).

PKDOC Program Accomplishments

PKDOC was started in 2010 to develop and obtain qualification of drug development tools (DDTs) from the US FDA and EMA for use in clinical trials for new therapies. To date PKDOC accomplishments include:

2013 — Development of a CDISC therapeutic area user guide (TAUG) for PKD

2015 — FDA Letter of Support for TKV "as measured by magnetic resonance imaging (MRI), computed tomography (CT), or ultrasound (US), and possibly in combination with other patient factors, as an exploratory prognostic biomarker for enrichment in clinical trials for autosomal dominant polycystic kidney disease (ADPKD)"

2015 — EMA positive qualification opinion for TKV as a prognostic biomarker to select patients for clinical trials of new therapies for ADPKD

2016 — FDA qualification of TKV as a prognostic biomarker from FDA in the form of Final Guidance

2018 — FDA designation of TKV as a reasonably likely surrogate endpoint

TKV as a Reasonably Likely Surrogate Endpoint

A reasonable likely surrogate endpoint is an "endpoint supported by strong mechanistic and/or epidemiologic rationale such that an effect on the surrogate endpoint is expected to be correlated with an endpoint intended to assess clinical benefit in clinical trials, but without sufficient clinical data to show that it is a validated surrogate endpoint" (FDA-NIH Biomarker Working Group, 2016).

In 2018, the FDA determined that TKV could be appropriate for use as a primary efficacy clinical trial endpoint for drug or biologic approval for patients with ADPKD or associated polycystic liver disease. TKV is appropriate for accelerated approvals and is mechanism agonistic (not directly related to the causal pathway).

The PKDOC has contributed to the PKD community by definitively demonstrating the clinical validity and usefulness of TKV, opening this measure for use in regulatory decision making (prognostic biomarker). PKDOC has also provided a quantitative model that can be used for the interpretation of TKV with respect to disease progression in clinical trials. Most importantly, the Consortium has enabled a new regulatory pathway (TKV as a reasonably likely surrogate endpoint) for demonstrating the effectiveness of new treatments for PKD increasing pharmaceutical company interest and investment in new PKD drug development.

Summary

PKDOC continues to define the unmet drug development needs for PKD and identify tools that could fill these needs to support therapeutic development for PKD patients. This includes the assessment of potentially useful biomarkers, clinical outcome assessments, and quantitative tools. As with our transformative work enabling TKV as a reasonably likely surrogate endpoint, PKDOC will continue to identify and align on the most important drug development needs and prioritize high impact solutions for formal regulatory endorsement for use in all stages of drug development. Furthermore, PKDOC will continue to explore opportunities to expand the application of tools in clinical practice to benefit patient care.

Team

John Michael Sauer, PhD
Program Officer, Translational and Safety Sciences
Executive Director, Polycystic Kidney Disease Outcomes Consortium (PKDOC)

Wendy T Vanasco
Senior Project Manager
Translational and Safety Sciences

Kitty Bogy
Project Coordinator
Translational and Safety Sciences

Email pkdocinfo@c-path.org with any questions.

References

- European Medicines Agency. Qualification opinion. Total Kidney Volume (TKV) as a prognostic biomarker for use in clinical trials evaluating patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) 2015.
- U.S. Food and Drug Administration. Table of Surrogate Endpoints That Were the Basis of Drug Approval or Licensure 2020b (accessed August 3, 2020).
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CRITICAL PATH INSTITUTE

1730 E. River Rd., Tucson, AZ 85718

520.547.3440

PKD FOUNDATION
Polycystic Kidney Disease