Up Next: Case Study 3: RDCA-DAP drug development tool prototypes—examples of the use of integrated rare disease data to accelerate drug development

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RDCA-DAP drug development tool prototypes:
Examples of the use of integrated rare disease data to accelerate drug development

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FDA qualification decision:

• Baseline TKV is a prognostic enrichment biomarker to select patients with ADPKD at high risk for a progressive decline in renal function (defined as a confirmed 30% decline in the patient’s eGFR), for inclusion in interventional clinical trials.
FDA reasonably likely surrogate designation:

- TKV could be used as a surrogate endpoint in an FDA accelerated approval process, with an acceptable plan for a post-marketing confirmatory trial would be required.
- TKV could potentially be accepted as an endpoint in and of itself (girth or size), but the bar for safety would be high, and the treatment effect would likely need to be large.
- Under a “Stratified Trial Design”, eGFR could be used as an endpoint when eGFR is declining more rapidly, while TKV could be used as an endpoint when eGFR is declining very slowly, and if there was an effect in both groups, a drug could receive approval for both populations.
- If the drug effect were significant enough to virtually halt cyst growth, TKV could be used as the endpoint in such a trial.
Quantitative solutions for PKD (beyond a surrogate)

**Input**
Clinical Data

**Transformation**
Disease Modeling

- Baseline severity
- Age
- Demographics
- Sex
- Genetics
- Medications
- Baseline biomarkers
- Longitudinal biomarkers
- Dropouts
- Longitudinal endpoints

**Output**
Actionable Knowledge

- Joint understanding of TKV+eGFR dynamics, and time-varying probability of eSRD
- Trajectory Rate Predictors
- Web Clinical Trial Simulator
The underlying patient-level data are very rich.

Patient-level data with high variability requires sophisticated quantitative approaches.

This allows the identification and quantification of sources of variability (genetics, demographics, baseline severity, comorbidities, concomitant drug use, etc.).
Clinical trial simulator for PKD

Joint modeling properly describes the relationship between TKV+eGFR dynamics and the time-varying probability of eSRD.

The multivariate model properly describes the data.

Next steps:
• Continuous expansion of the PKD patient-level data sources in RDCA-DAP
• Continuous collaboration between RDCA-DAP and PKD-OC
• Complete a clinical trial simulator for PKD
• Submit for regulatory review and potential endorsement
Data Interoperability solutions: PKD and kidney transplant – eGFR profiles

- Understanding data across indications
- Provides valuable learnings for other efforts
- Can inform solutions for drug development in PKD and kidney transplant therapeutics

*eGFR units in ml/min/1.73m²*
Meaningfully exploring patient-level data in Friedreich’s ataxia

- User friendly interfaces democratize the ability of researchers to interact with data
- Provides valuable learnings across RDCA-DAP
- Can form the basis for the generation of comprehensive plans to develop tangible drug development solutions
Meaningfully exploring patient-level data in Friedreich's ataxia

User friendly interfaces democratize the ability of researchers to interact with data

Provides valuable learnings across RDCA-DAP

Can form the basis for the generation of comprehensive plans to develop tangible drug development solutions
Meaningfully exploring patient-level data in PKU

- User friendly interfaces democratize the ability of researchers to interact with data
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Kidney transplantation:
Data interoperability maximizes the information value of the patient-level data across indications. Gained insights provide the potential for optimized medical product development beyond a single indication.

Polycystic kidney disease:
Biomarker dynamics model coupled with disease progression model that facilitated the approval of the first-ever treatment to slow disease progression, also solidifying a pipeline of over ten novel drugs under development.
Now taking the next step to expand the set of quantitative solutions, to accelerate medical product development in PKD even more.

Friedreich’s ataxia and phenylketonuria:
A patient-level data foundation has been laid, on top of which quantitative insights can be gained, aiming to accelerate medical product development for individuals in need.
THANK YOU!

Don't forget to answer survey questions.

For more information, email rdcadap@c-path.org