Transforming Clinical Care in Polycystic Kidney Disease

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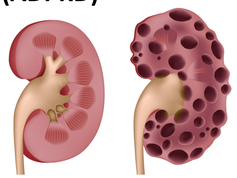
Background

Autosomal Dominant Polycystic Kidney Disease (ADPKD)

- Most common hereditary kidney disease
- 4th leading cause of kidney failure
- Due to mutations of *PKD1* or *PKD2* gene
- Uncontrolled growth of fluid-filled cysts causes irreversible kidney damage
- The only currently approved drug, Tolvaptan, is expensive and associated with significant side effects



Study Aims

1.2

- Create a national clinical trial network
- Test 400 patients using genetic and kidney volume based risk assessment tools, while evaluating the use of:
  - Next generation sequencing for genetic testing
  - 3D-ultrasound (US) for kidney volume measurement

2.1

- Pilot clinical trial on a promising repurposed drug (Salsalate) using the high risk patient cohort identified in Project 1.2

Methods

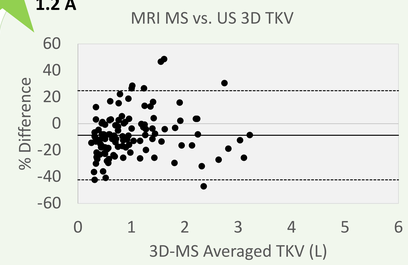
PKD Study Centres

- University Health Network – Toronto, ON
- St. Joseph's Healthcare Hamilton – Hamilton, ON
- London Health Sciences Centre – London, ON
- The Ottawa Hospital – Ottawa, ON
- Centre de Recherches – Montreal, QC
- University of Alberta – Edmonton, AB
- St. Paul's Hospital – Vancouver, BC

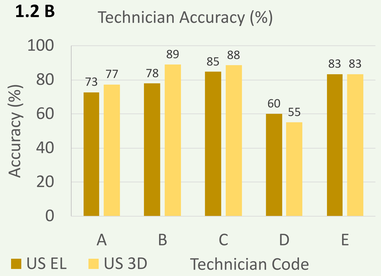
Results

1.2

1.2 A



1.2 B

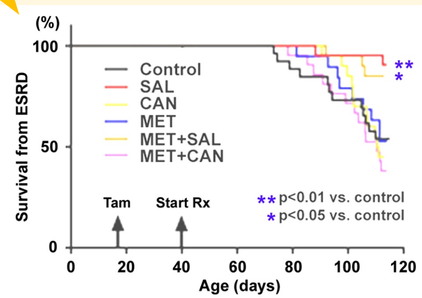


1.2A 3D-US has a higher error rate when compared to the gold standard of MRI, and measures an accuracy of 79% (based on Mayo Clinic Imaging Classification [MCIC])

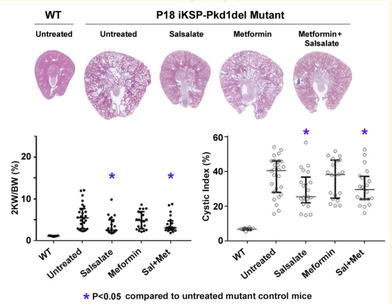
1.2B Kidney volume measurement via US is dependent on technician bias

2.1

2.1 A



2.1 B



2.1A&B Preclinical animal studies identify Salsalate as a promising repurposed drug for treatment of ADPKD

Project Timeline

1.2

- 2016: Develop protocols, consents, and data transfer agreements/contracts
- 2017: Obtain approval for Research Ethics and contracts departments (Ongoing)
- 2018: Patient Recruitment (P.E)
- 2021: Data collection (Saliva, MRI, and 2 Questionnaires) (P.E)
- 2022: Data analysis; Knowledge sharing: conference presentations and publications (P.E)

P.E Patient Engagement

Project Timeline

2.1

- 2019: Preclinical testing completed
- 2019: Develop protocol and consent for small Salsalate pilot trial (P.E)
- 2021: Execute trial (P.E)
- 2022: Analyze, share results and knowledge (P.E)

P.E Patient Engagement

Accomplishments to Date

1.2

- 120 patients studied for 3D Ultrasound project, which is nearing completion
- ~ 416 patients enrolled for clinical trial network
- Web-based ADPKD questionnaires & 7 active sites.

2.1

- Preclinical animal studies supporting use of Salsalate in Project 2.1; manuscript submitted for publication
- Research Ethics Board (REB) approval for Salsalate clinical pharmacokinetic study in patients

Next Steps

- Complete patient risk assessments from all study sites
- Analyze imaging to validate the use of 3D-US in ADPKD risk assessment
- Short-term pilot study to examine the pharmacokinetics, safety, and tolerability of Salsalate in patients
- Potential use of Salsalate to reduce urine output in Tolvaptan-treated patients

Future Opportunities for Patient Engagement

- Quarterly teleconference calls
- Feedback on trial design and consent for 2.1
- Contributors to future manuscripts and presentations
- Knowledge sharing

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