Key Information on Upcoming Clinical Trials

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Clinical Trials: A Brief Primer

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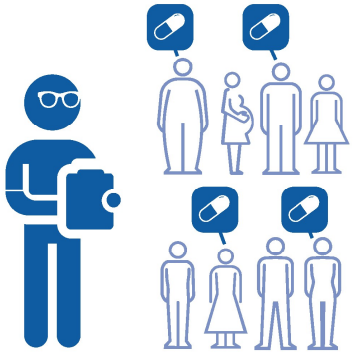
What is the main difference between the types of clinical research studies?

The main difference is if researchers assign participants to get an **intervention**, such as a drug, behavior, or medical device.

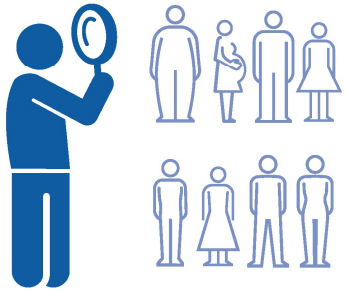
Clinical trial



In **clinical trials**, researchers do **assign participants** to one or more interventions.

Sometimes, researchers randomly assign participants to interventions.

Observational study



In **observational studies**, researchers **do not assign** participants to an intervention.

If there is an intervention, participants were already using it as part of their regular health care or daily life.

Clinicaltrials.gov

Eligibility Criteria

- The key requirements that people who want to participate in a clinical study must meet or the characteristics they must have.
- Eligibility criteria consist of both **inclusion criteria** (which are required for a person to participate in the study) and **exclusion criteria** (which prevent a person from participating).
- Types of eligibility criteria include whether a study accepts healthy volunteers, has age or age group requirements, or is limited by sex.

Clinicaltrials.gov

Informed Consent

- A description of what will happen during the study
- Who can join the study
- How much of participants' time the study will take
- Any payments and costs, such as payment participants get from taking part and any costs participants may need to pay
- The known benefits and risks of taking part in the study

Clinicaltrials.gov

Randomization

- Researchers assign participants to interventions randomly.
- This means that researchers assign the participants by chance.
- Participants (or their doctors) don't choose what intervention they will get when they join a clinical trial.

Clinicaltrials.gov

Potential Benefits of Taking Part in Clinical Research

- Help researchers learn about health, illness, or treatments
- Be a part of discovering health information that may help others in the future
- Possibly get a drug or medical device that is not yet approved to be used in people with a certain health condition
- Participants may or may not get any benefit themselves from joining a clinical research study.
- In clinical trials, researchers often don't know if the intervention will be helpful, harmful, or the same as regular health care.

Clinicaltrials.gov

Possible Risks of Taking Part in Clinical Research

- The chance that participants will have a side effect or other health problem during a study (also called an adverse event)
- Participants may not get the intervention being tested in a clinical trial – instead, they may get the standard treatment or no treatment at all
- The intervention being tested may not work better than the standard treatment
- The study may require more time and visits than their regular health care

Clinicaltrials.gov

Phases of Clinical Trials

Pre-Clinical: Studies in animals to test safety, efficacy, dosing, drug kinetics (e.g. peak and duration of activity, time to elimination)

Phase I: Tests the safety and dosage of a new drug or treatment in a small group of healthy volunteers (20-100).

Phase II: Focuses on the efficacy of the drug, assessing its effectiveness and side effects in a larger group (100-300) of participants.

Phase III: Involves a larger population (1,000- 3,000) to confirm effectiveness, monitor side effects, and compare it to commonly used treatments.

Phase IV: Conducted after the drug is approved, this phase monitors long-term effects and effectiveness in the general population.

Adapted from: Step 3: Clinical Research | FDA

Clinical Trial Opportunities

Currently Enrolling

Anchor (Abbvie-CLS-628)

Phase 2 (NCT06902558)

Sites: National

Aglow (Vertex – VX-407)

Phase 2 (NCT07161037)

Sites: National

Enrolling later in 2026

BEAT-PKD (Bempedoic Acid)

Phase 2 (NCT07282821)

Sites: Tufts, U. Vermont, U. Maryland

Farabursen (anti miRNA17)

Phase 3 (NCT pending)

Sites: TBD

Who is eligible, generally, specifics to follow…

Inclusion

- Confirmed ADPKD
- Age 18+ (upper age limit 55-65, varies by study)
- eGFR lower limit ≥ 25-35 ml/min/1.73m^2 (varies by study)
- eGFR upper limit varies by study
- Mayo Imaging Class (MIC) 1C-E (or 1B with eGFR decline >3 ml/min/year in BEAT-PKD)

Exclusion

- Diabetes
- Kidney disease other than ADPKD
- Prior cyst reduction surgery
- Others vary by study

AGLOW trial
Vertex-101

Craig Gordon, MD, MS
Division of Nephrology
Tufts Medical Center

Aglow: for individuals with non truncating mutation in specific region of PKD1

VERTEX

VERTEX PHARMACEUTICALS INCORPORATED

Clinical Study Protocol

A Phase 2a, Open-label, Single-arm Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of VX-407 in Subjects with Autosomal Dominant Polycystic Kidney Disease Who Have a Subset of PKD1 Gene Variants

Vertex Study Number: VX24-407-101

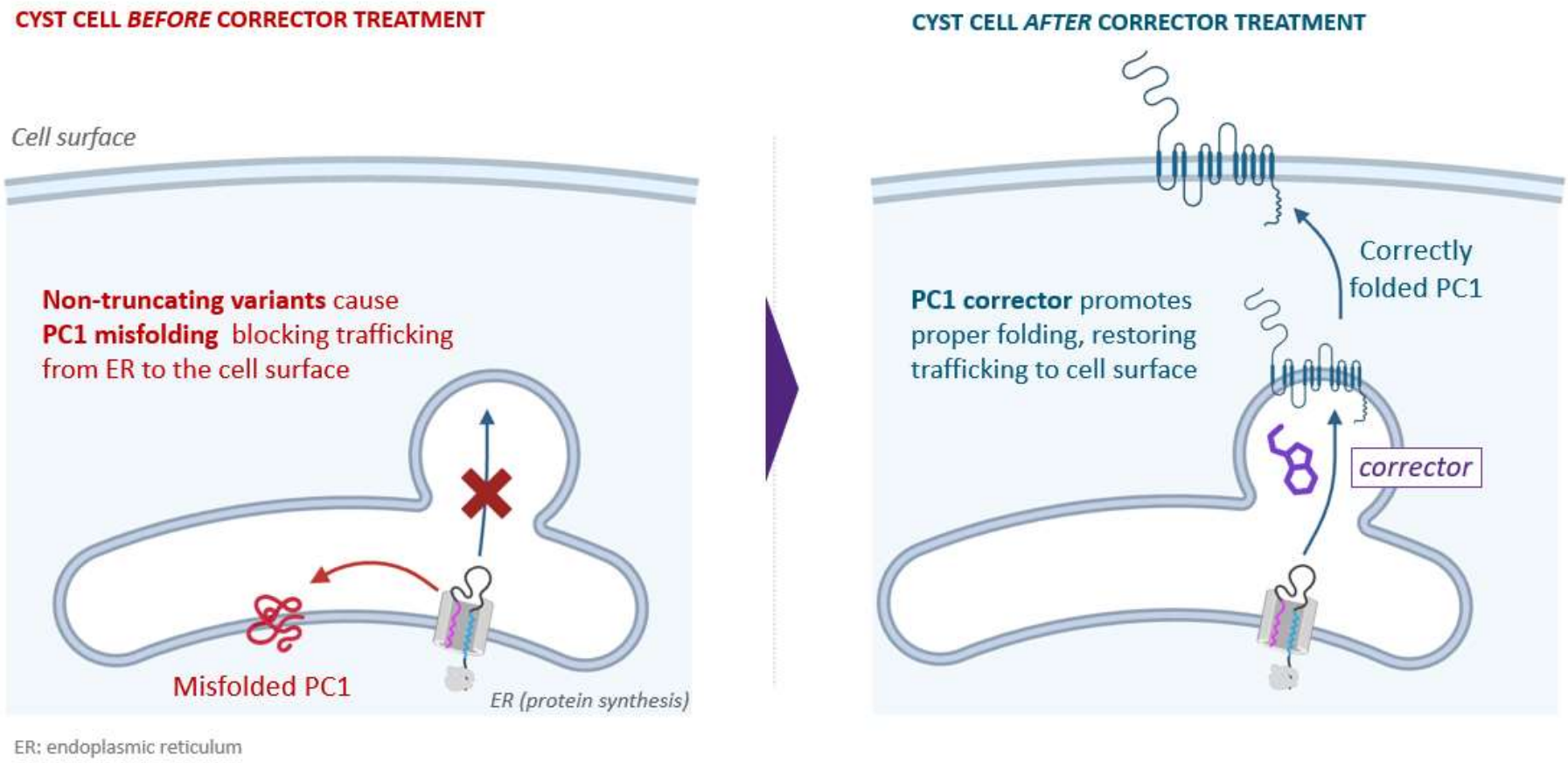
IND Number: 169216

CTIS: 2024-517393-13-00

- Phase 2a Study
- 24 patients
- Open Label
- **Oral therapy**

PC1 CORRECTORS AIM TO RESTORE FOLDING & TRAFFICKING TO CELL SURFACE

TARGETING ADPKD PATIENTS WITH NON-TRUNCATING VARIANTS IN *PKD1*



Courtesy of Vertex Pharmaceuticals, Inc.

Aglow (Vertex-101)

- Study begins with genetic testing
- Determine if individual has non-truncating mutation in specific region of *PKD1*
- Genetic testing only in individuals who meet inclusion criteria and willing to participate in trial
  - Age 18-65
  - Mayo 1C-1E (and 1B if htTKV >250 ml/m)
  - eGFR ≥ 25 ml/min/1.73m2
- Visit Frequency: Every 4-6 weeks for one year
- Study drug: pill taken orally, no placebo

ANCHOR study
Inhibition of Pregnancy Associated Plasma Protein-A (PAPP-A)

Ronald Perrone, MD

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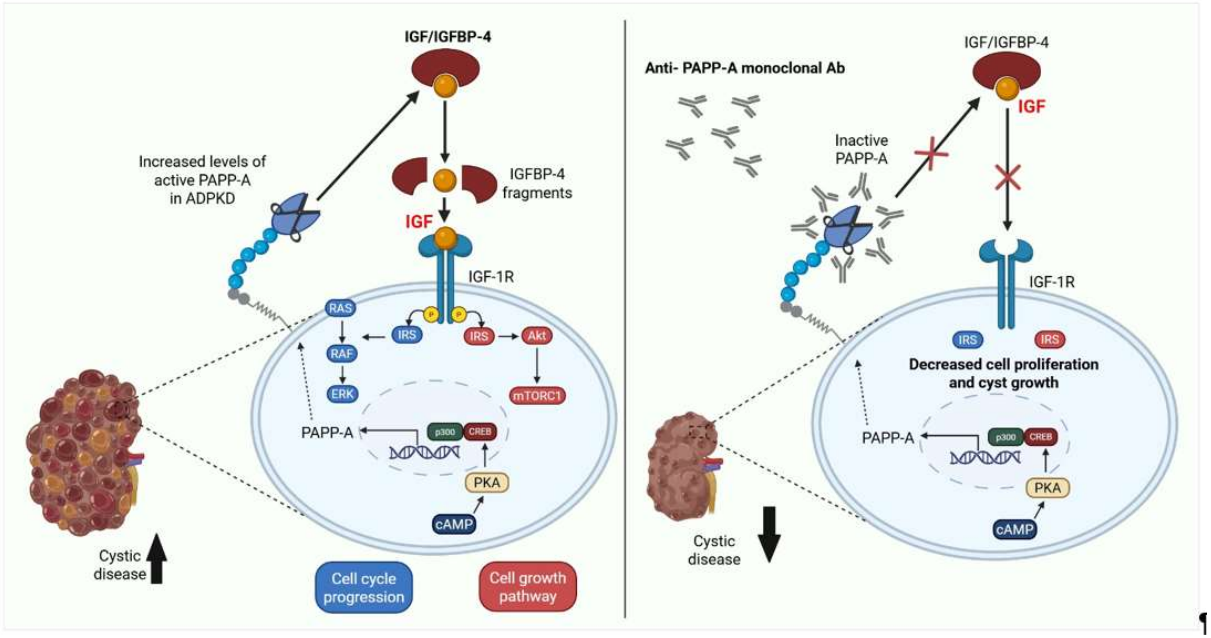
Anchor Study: Inhibition of Pregnancy Associated Plasma Protein-A

- PAPP-A is a secreted metalloproteinase that increases tissue IGF bioavailability by cleaving the inhibitory IGFBPs.

Insulin like growth factor (IGF) is a potent signaling pathway that mediates cell proliferation, apoptosis, differentiation, migration.



Chen et al, Kidney 360, 12/25

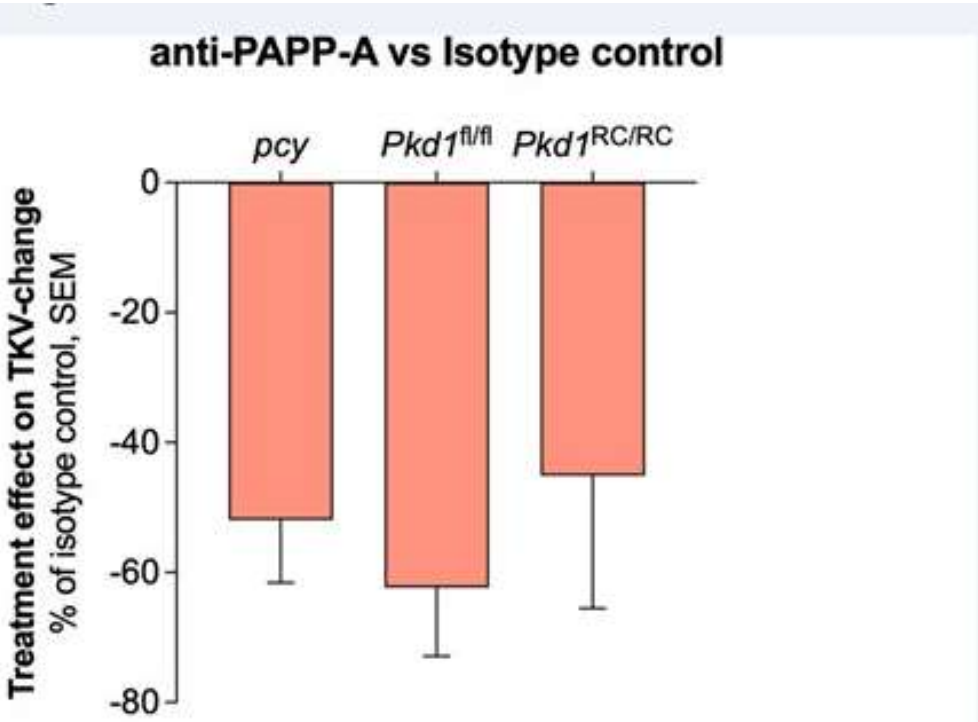


Figure 1: *Mean reduction in total kidney volume (TKV) enlargement from anti-PAPP-A treatment, compared to control, in three mouse models of ADPKD.*

Koukos, G et al. *Nephrology Dialysis Transplantation*, Volume 40, Issue Supplement_3, October 2025, gfaf116.036, https://doi.org/10.1093/ndt/gfaf116.036

abbvie

Protocol for Study M25-147

Autosomal Dominant Polycystic Kidney Disease: A Study of ABBV-CLS-628 in Adult Subjects with Autosomal Dominant Polycystic Kidney Disease

- Phase 2 Study of M25-147, a fully humanized IgG1 against PAPP-A
- Monthly IV administration study drug (900 or 400 or 100 mg vs. Placebo)
- Inclusion Criteria:
  - Age 18-55
  - MAYO 1C-1E
  - eGfr ≥ 30 and < 90 ml/min/1.73m2
- Study visits every 4 weeks
- 2 year follow-up
- Primary Outcome: Rate of Change in TKV at week 96

BEAT-PKD trial

Bempedoic acid

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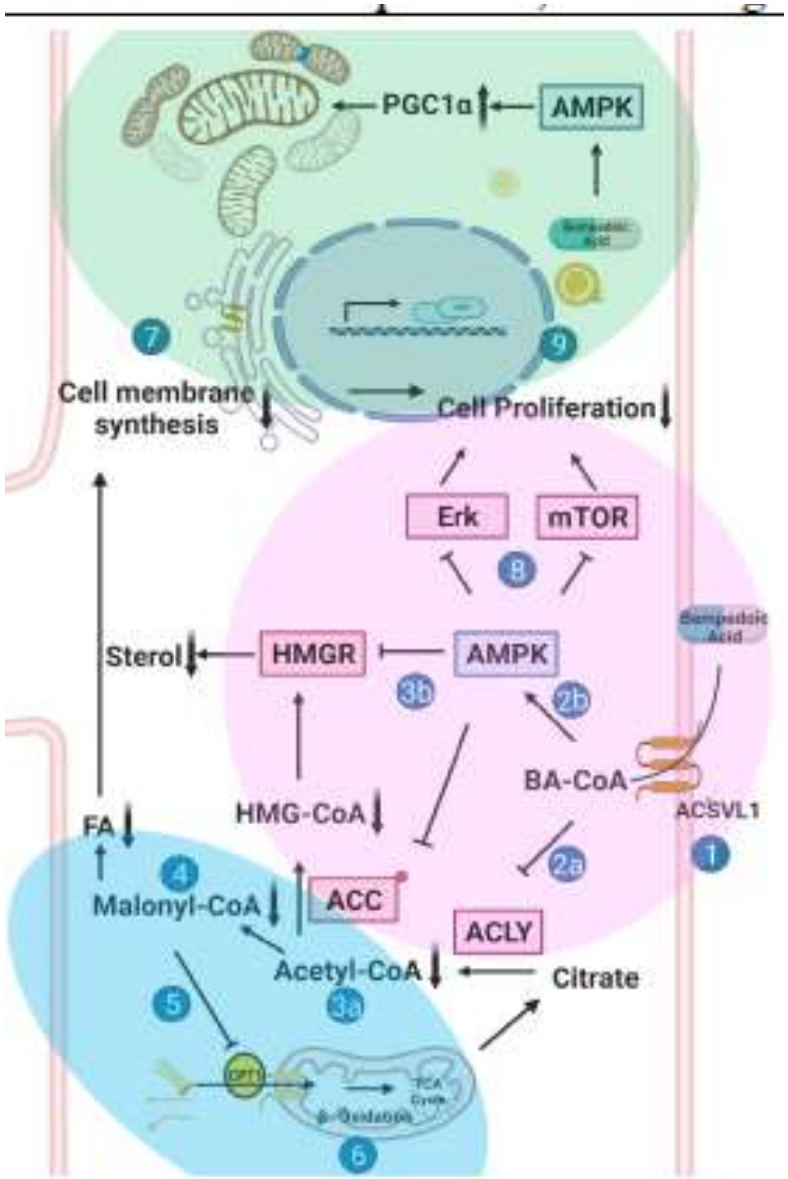
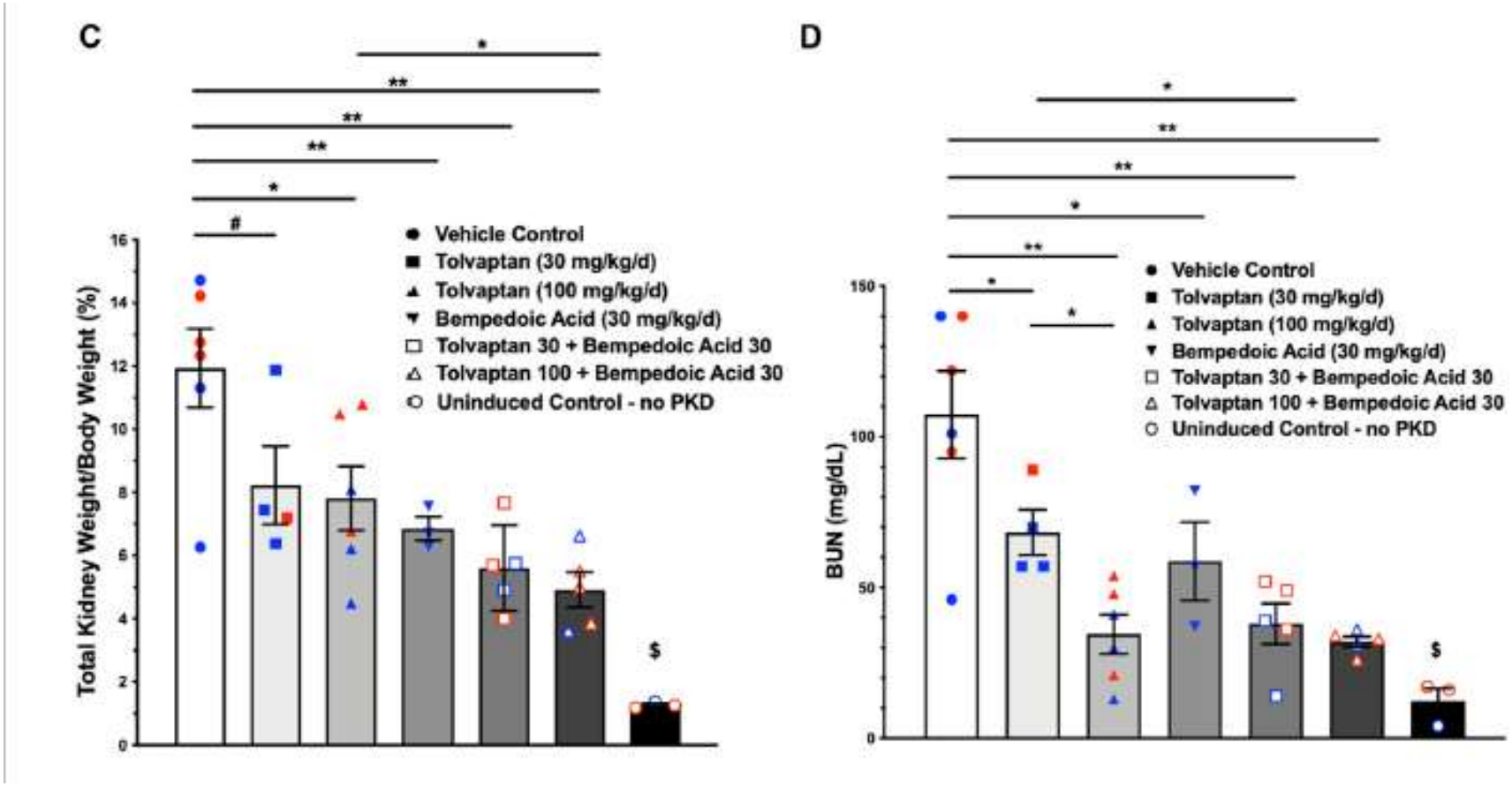


BEAT-PKD (Bempedoic Acid)

AMPK Activation- inhibits cell cycle initiation (ErK, mTOR)
Decreased sterol and fatty acid synthesis

Hallows, K Front Mol Biosci 2022

Effects in Mice Independent of and in Addition to Tolvaptan



Hallows K et al. Frontiers Molec Biosciences 2022

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 13, 2023 VOL. 388 NO. 15

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

S.E. Nissen, A.M. Lincoff, D. Brennan, K.K. Ray, D. Mason, J.J.P. Kastelein, P.D. Thompson, P. Libby, L. Cho, J. Plutzky, H.E. Bays, P.M. Moriarty, V. Menon, D.E. Grobbee, M.J. Louie, C.-F. Chen, N. Li, L.A. Bloedon, P. Robinson, M. Horner, W.J. Sasiela, J. McCluskey, D. Davey, P. Fajardo-Campos, P. Petrovic, J. Fedacko, W. Zmuda, Y. Lukyanov, and S.J. Nicholls, for the CLEAR Outcomes Investigators*

Bempedoic acid is approved by both the United States (US) Food and Drug Administration (FDA) and the European Medicine Agency for the treatment of hypercholesterolemia as a single agent and as a fixed dose combination therapy with ezetimibe.

This is an example of drug repurposing!

BEAT-PKD

- 3 clinical sites (University of Vermont (Hallows), University of Maryland (Seliger/ Watnick), Tufts (Miskulin/ Gordon/Perrone) DCC (UPMC, Abebe)
- 120 patients (40 from each site)
- 2 year follow up
- Randomized, Double Blinded
- Intervention: Bempedoic Acid 180 mg po daily or placebo
- Primary Outcome: safety, tolerability
- Secondary Outcome: TKV, eGFR, visceral fat, metabolic markers

BEAT-PKD

- This is the only therapeutic trial that allows concomitant tolvaptan use (stable dose for 3 months)
- Inclusion Criteria:
  - Age 18-60
  - MAYO 1C-1E, or 1B w/ eGfr decline >3 ml/min/yr
  - eGfr ≥ 35 ml/min/1.73m2

Farabursen Trial

Novartis (details not yet available)

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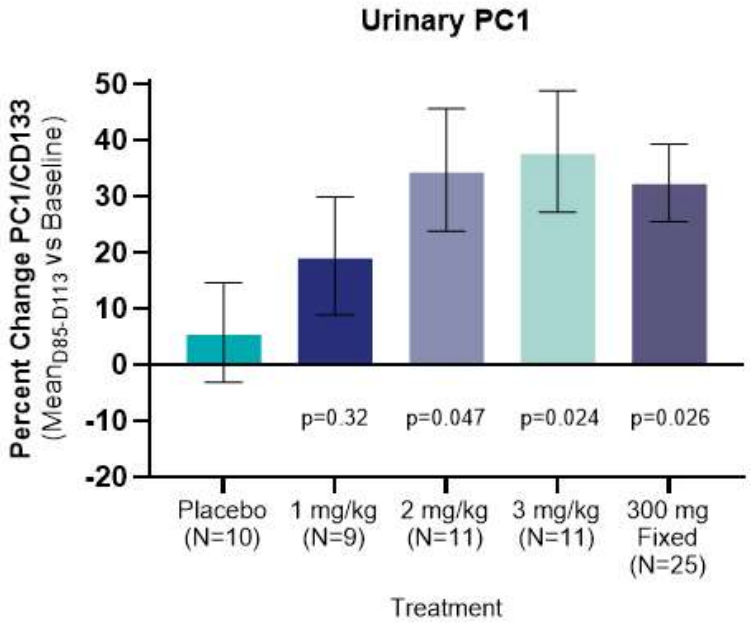
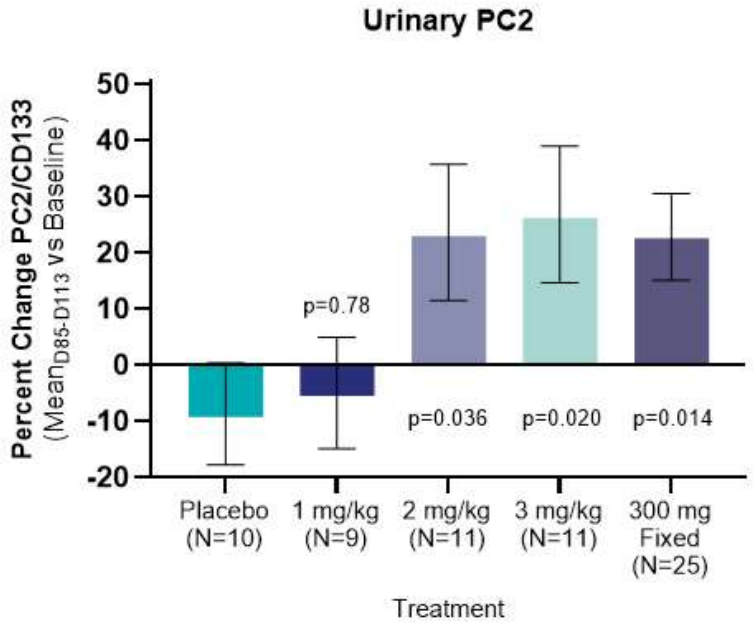
Block Inhibitory Effect of microRNA17 on PC1 Expression

- MicroRNAs (miRNAs) are non-coding RNAs that bind to complementary sequences located in target mRNAs and inhibit their expression
- miRNA 17 is upregulated in kidney cysts (mouse and human)
- Deletion of miRNA 17 attenuates cyst growth (mouse)
- Anti-miR-17 demonstrates therapeutic efficacy in short-term and long-term PKD mouse models.

Final Cohort 4 Data Continue to Demonstrate Evidence of Maximal Mechanistic Activity with a 300 mg Fixed Dose



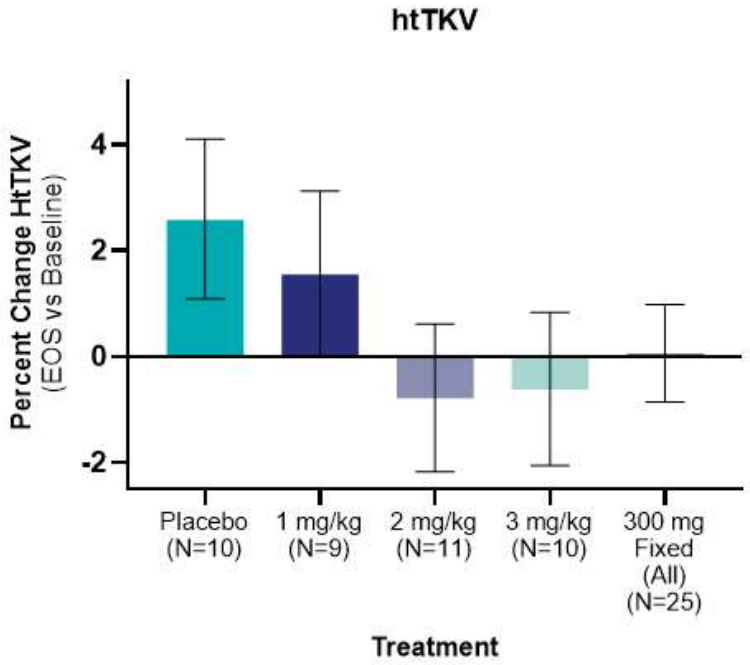


Geometric least squares mean percent change data shown. Error bars represent standard errors. ANCOVA analyses performed on log scale transformation to account for non-normal distribution. Data not available for one subject in each of 3 mg/kg and 300 mg/kg Fixed groups.

Oral presentation, SA-OR89 ASN Annual Meeting 2025, Houston, Tx

Final Cohort 4 Data Continue to Demonstrate Evidence of Reduction in htTKV Growth Rate with a 300 mg Fixed Dose

Changes in htTKV were highly correlated with changes in kidney cyst volume



Geometric least squares mean percent change data shown. Error bars represent standard errors. ANCOVA analyses performed on log scale transformation to account for non-normal distribution. EOS, End of study. Data not available for two subjects in 3 mg/kg group and one subject in 300 mg Fixed group. One subject in 300 mg/kg Fixed group with renal cyst rupture includes only contralateral kidney results.

REGULUS

Farabursen (Novartis)

- Phase 3 Study: full details pending
- 2 year study duration (presumed)
- Subcutaneous injection every 2 weeks

Study Contacts

- PKD Navigator: Gabrielle Cournoyer
- (617) 636-8117 Gabrielle.Cournoyer@tuftsmedicine.org

- BEAT Research Study Coordinator: Shuaib Mohammed
- (617) 636-2609 Shuaib.Mohammed@tuftsmedicine.org

- Clinical Study Unit Research Coordinator: Olaniyi (Niyi) Ogunbodede
- (617) 636-5076 Olaniyi.Ogunbodede@tuftsmedicine.org

Time for Questions