CLINICAL STUDIES: PATIENT PARTICIPATION IS KEY IN DEVELOPING TREATMENTS

The PKD Foundation believes empowered patients are the key to accelerating the development of a robust treatment pipeline. Without participation in research, medical breakthroughs cannot happen and new therapies cannot be approved for patient use.

Progress to find treatments for polycystic kidney disease is partially driven by patient involvement in clinical studies. According to clinicaltrials.gov, “A clinical study involves research using human volunteers that is intended to add to medical knowledge.”

For more information and videos, visit pkdcure.org/clinicalstudies.

PKD FOUNDATION
Polycystic Kidney Disease

pkdcure.org
1.800.PKD.CURE
A clinical study involves research using human volunteers (participants) that is intended to add to medical knowledge. There are two types.

**OBSERVATIONAL STUDIES**
Data is collected but there is no attempt to alter the disease progression.

- Provides clinical information about disease progression
- **YOU MIGHT:**
  - Write in a journal
  - Talk with a doctor
  - Keep a food diary
  - Have your blood pressure taken

**CLINICAL TRIALS**
A drug is given or a device is used to alter the course of the disease.

- Evaluates effectiveness of an intervention to slow or stop a disease
- **YOU MIGHT:**
  - Take a pill/drug
  - Have a procedure done
  - Use a device
  - Change your diet

**Example:**
Consortium for Radiologic Imaging Studies of PKD (CRISP)

**Example:**
Tolvaptan TEMPO ¾ Trial
Finding Treatments: Patient Participation is Key

There are two types of studies and patients can participate in many ways. These include:

- **Observational Studies** monitor and record various clinical and/or subjective factors over a period of time, like blood pressure or quality of life, to better understand how the disease progresses. Involvement includes activities such as having conversations with researchers and physicians, or recording daily events in journals. No drugs are given or other interventions* are made to alter the course of the disease. An example of an observational study is the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP).

- **Clinical trials** monitor and record various clinical and/or subjective parameters by testing experimental treatments, devices or combinations of drugs that may alter the course of the disease. Participants receive specific interventions* which may be medical products such as drugs or devices; procedures; or changes to participants’ behavior such as diet. The purpose of a clinical trial is to test a new drug or other intervention for safety and effectiveness in treating the disease in question before it can be prescribed for patients. An example of a clinical trial is the Tolvaptan TEMPO ¾ Trial.

*According to clinicaltrials.gov, an intervention is a process or action that is the focus of a clinical study. This can include giving participants drugs, medical devices, procedures, vaccines, and other products that are either investigational or already available. Interventions can also include noninvasive approaches such as surveys, education and interviews.

**What to Know About Participating in Clinical Studies**
Participating in a clinical study can be a very satisfying and worthwhile experience. The results can make a difference in the care of future patients by providing information about the benefits and risks of therapeutic, preventative, or diagnostic products or interventions.

By participating in a clinical study, you can:
- Play a more active role in your own health care.
- Have access to new treatments before they are available to the public.
- Contribute to the development of treatments for PKD.
- Make things better for the next generation of those with PKD.

It is important that any participation should be done in consultation with your health care provider. To participate in a clinical study, you will need to have a formal diagnosis of PKD made by a physician.

Anyone interested in participating in a study should know as much as possible about the study and feel comfortable asking the research team questions. There are processes in place to protect patients, such as the informed consent process. It involves researchers communicating with potential and enrolled patients about a clinical study, providing all the important information about the study, ensuring potential participants understand the risks and benefits and stress that enrollment is strictly voluntary. All important information about a study must be given to the potential participant in a written document that is easily understood. Typically, a person must sign an informed consent form to participate. For more information on this process and a list of sample questions to ask, visit clinicaltrials.gov.

With thousands of people living with PKD in the U.S. alone, clinical study participation can provide help and hope to those affected by PKD.
Awareness and Drop-outs the Biggest Challenges for Successful Studies

**Awareness**
The greatest hurdles for successful studies are low recruitment due to lack of awareness, and participants dropping out before the study is complete.

According to a report from the National Institutes of Health (nih.gov/health/clinicaltrials/providers/awareness.htm) that compiled several studies:
- 85% of patients were either unaware or unsure that participation in a clinical trial was an option at the time of diagnosis.
- 75% of these patients said they would have been willing to enroll had they known it was possible.

Today, approximately **80 percent of all clinical trials fail** to recruit enough volunteers within planned timelines. Under-enrollment is potentially one of the most significant problems facing PKD drug development.

In 2010, to address this awareness challenge, the PKD Foundation launched the **Clinical Trials Awareness Program (CTAP)**, an aggressive program to help create awareness amongst patients and families and speed up clinical trial recruitment. The program is focused on educating patients about current studies so they can make educated decisions about participating. The goal is to simplify the process of finding clinical studies for PKD patients in their geographic area by sending Accelerating Clinical Trials (ACT) Alert emails about studies that are being conducted.

Traditionally, the pharmaceutical industry leverages mass media, like television, radio and print advertising, to inform patients about clinical trials. To reach the national, widely dispersed PKD community in this way is expensive and not an effective use of funds. This makes it difficult for PKD patients to be made aware of opportunities to consider clinical trial participation.

Recently, ACT Alerts focused on two clinical trials that were enrolling ADPKD patients. **Thirty-six thousand emails were sent out six times over a three-month period with an average of 14 percent of recipients opening the emails.** The organization conducting the trials used a questionnaire to gain insights from participating patients, and nearly **80 percent of the 416 respondents learned about the trial from the Foundation’s ACT Alert.**

To receive ACT Alerts, please visit pkdcure.org/email-preferences, enter your information and check the ‘Clinical Trials and Research’ button.

**Participation and Dropping Out**
When designing a clinical study, the study research team determines the number of participants needed for enrollment in order to measure a significant effect of the intervention. While drop outs can’t always be avoided, it does impact the results if enrollment numbers drop below what is needed for study significance. Participants should discuss study requirements with their health care provider and members of the research team before enrolling to ensure expectations are understood and can be met.
Phases of a Clinical Trial

The U.S. Food and Drug Administration (FDA) is the federal agency charged with oversight of all the clinical trials going on in the U.S. at any time. A new drug to treat PKD must move through each stage before it can be reviewed for approval by the FDA. The FDA defines the phases for the clinical trials.

- **Phase I** – The new drug is tested for safety and side effects in a small number of healthy volunteers with PKD.
- **Phase II** – The new drug is tested for safety, dose ranging and preliminary effectiveness in a small number of volunteers.
- **Phase III** – The new drug is tested in a large number of volunteers with PKD to establish effectiveness, monitor side effects and compare results with current treatments.

- The data collected during the clinical trial is analyzed and then submitted to the FDA for regulatory review, which can take one to three years. If there is an intent to apply for an NDA (new drug application), it is communicated to the FDA and shapes the design of the study. Once it is approved, the new drug can be prescribed by physicians to treat PKD. (See Page 8 about the tolvaptan NDA).
- **Phase IV** – These studies are done after the drug has been approved by the FDA and it is in use (considered a post-marketing study). Additional information about risks, benefits and optimal use is collected and analyzed.

CLINICAL STUDIES FOR PKD TREATMENTS

In the U.S., there are more than **30 clinical studies related to PKD** that are currently active or recruiting for participation. For more information on these studies, visit [pkdcure.org/clinicalstudies](http://pkdcure.org/clinicalstudies). Clinical studies are critical and a required step to the development of new therapies.
FDA’S DRUG APPROVAL PROCESS

1. Drug compound developed by drug sponsor.

2. Preclinical animal testing to gather information on safety and effectiveness.

3. An investigational new drug (IND) application outlines what the sponsor of a new drug proposes for human testing in clinical trials.

4. Phase 1 studies (typically involve 20 to 80 people). This phase emphasizes safety.

5. Phase 2 studies (typically involve a few dozen to about 300 people). This phase emphasizes effectiveness.

6. Phase 3 studies (typically involve several hundred to about 3,000 people). This phase gathers further information about safety and effectiveness through different populations and dosages.

7. The pre-NDA period, just before a new drug application (NDA) is submitted. A common time for the FDA and drug sponsors to meet.

8. Submission of an NDA is the formal step asking the FDA to consider a drug for marketing approval.

9. After an NDA is received, the FDA has 60 days to decide whether to file it so it can be reviewed.

10. If the FDA files the NDA, an FDA review team is assigned to evaluate the sponsor’s research on the drug’s safety and effectiveness.

11. The FDA reviews information that goes on a drug’s professional labeling (information on how to use the drug).

12. The FDA inspects the facilities where the drug will be manufactured as part of the approval process.

13. FDA reviewers will approve the application or issue a complete response letter (CRL). See the first paragraph in the update on page 8 for more information about CRLs.

14. Once the FDA approves a drug, the post-marketing monitoring stage begins to detect serious unexpected events and take action when needed. Drug can now be prescribed to patients.

Source: fda.gov
But what really shook Margot was when her daughter Lena was diagnosed at age nine. She is now 15, a teenager trying to lead a normal life. “I felt terrible when I found out Lena had PKD,” Margot said. “She was checked in utero and had been cleared, but when her later hypertension revealed she had it, I just burst into tears. I don’t think any parent feels good about passing on a life-threatening illness to their child, and I was no exception.”

Lena took it well for a nine-year-old. “I knew my mom had it and she seemed okay, so I wasn’t too worried.” But PKD takes a toll on both mother and daughter. Margot works hard to watch her diet and exercise, and feels pretty good physically, but emotionally and logistically PKD has dramatically changed her lifestyle. Lena hasn’t told most of her friends at school for fear they will treat her differently. It is important to Margot to be a role model for Lena about how to take care of herself and live a fulfilled life with PKD.

One way the Keys family works to be their own best advocates is to connect with the PKD Foundation. Margot and Lena attended United on the Hill (the PKD Foundation’s advocacy event) in June and participated in the Philadelphia Walk for PKD in September. Bill, Margot’s husband, ran in the Marine Corps Marathon in October as part of the Run for PKD program (runforpkd.org).

The Keys also arm themselves with as much information as possible. One way they do this is by taking part in clinical studies. “I highly recommend participating in clinical studies because you find out a lot about yourself and your own disease,” Margot said. “I participate to learn about what I can do to take care of myself, such as exercising, getting support and managing stress. Without being armed with information, you are just sitting and waiting when you may be able to change the outcome.”

Margot is in an observational study at the Hospital of the University of Pennsylvania. The goal of the study is to follow PKD patients over time to understand more clearly how the disease progresses, and if there are any notable trends over time. She goes in often for routine appointments for blood work, MRIs of her kidneys and physical examinations.

Lena is in the LEAPP Program through the Children’s Hospital of Philadelphia. LEAPP stands for Longitudinal Experience to Appreciate Patient Perspectives. The program involves two first-year medical students being assigned to patients with serious chronic illnesses, who they will keep in contact with for several years to understand how a chronic illness can affect a patient’s life, work and family. In this program, Lena will be the teacher and the medical students will learn from her.

Margot encourages others with PKD to get involved with clinical studies. “It is important to participate in studies because it helps all of us and future generations to know more about PKD,” Margot said. “It is a generational disease. If you won’t do it for yourself, do it for your kids. Until there is a cure, it helps to address the disease and find out more about how to live our best lives.”
Since its founding in 1982, the PKD Foundation has invested more than $32 million in research, clinical and scientific grants, as well as fellowships and scientific meetings, making us the second largest funder of PKD research after the National Institutes of Health (NIH).

Our focus is Accelerating Treatments to Patients (ATP), an initiative dedicated to facilitating the development of therapies for PKD.

The ATP initiative is a comprehensive, integrated research and development program that represents the core of our work. ATP was launched in 2010 to speed up development of treatments which could slow or stop the progression of PKD. Each of the programs within ATP is important and interconnected.