Clinical Trials: Why YOU Should Participate

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• The disease of polycystic kidneys in adults …… first shows signs or symptoms after the age of 30-40, and progresses mercilessly ……

• The genetically determined disease process is latent for many years, and then becomes manifest in a kidney tissue which has apparently developed and functioned normally.
ADPKD is a Slowly Progressive Kidney Disease

• Filtration (GFR) stable for many years; more rapid decline after 50% of function is lost
  Males 5 - 6 ml/min/year; Females 4 - 5 ml/min/year

• 50% of patients require dialysis/transplant by age 60
Early Stage of Cystogenesis

Baert, Kid. Int.
13:519, 1978
Renal survival

Proportion of patients (%)

PKD1

PKD2

Age (years)

0 20 40 60 80 100

Hateboer N; Lancet 353:103, 1999
How Do We Find Treatments For PKD?

• Develop new drugs
  – Based on laboratory and clinical research sponsored by institutions, PKDF, NIH, VA, DOD, Pharmaceutical industry

• Use existing drugs in a new way: repurpose
  – Based on laboratory and clinical research sponsored by institutions, PKDF, NIH, VA, DOD, Pharmaceutical industry
New Haven, Conn. — A treatment for polycystic kidney disease (PKD), a leading cause of fatal kidney failure worldwide, has been identified by a research team led by Yale biochemist Craig Crews, according to a report in the Proceedings of the National Academy of Sciences.

Over 12 million people worldwide suffer from PKD, a genetic disorder that causes uncontrolled growth of cells lining tubules in the kidneys, and results in the formation of many, large fluid-filled cysts in the kidneys.

“Unfortunately, aside from kidney transplantation, there has been no cure for PKD, nor has there been a suitable drug treatment to slow its progression,” said Crews, associate professor of chemistry, molecular, cellular & developmental biology and pharmacology. “We hope that is about to change,” he said.

The mesh of Traditional Chinese Medicines (TCMs), current advances in chemistry and fundamental processes of developmental biology and health are a research focus for Crews. According to him, a roadblock in the path to TCMs as a source for new medical treatments is lack of understanding the biology and chemistry of how they work.

Triptolide is a potent, biologically active compound isolated from the medicinal ‘Thunder God Vine’ Tripterygium wilfordii Hook F. The TCM tea Lei Gong Teng made from this plant has been used for centuries, as a therapeutic against cancer, inflammation, and auto-immune diseases. Crews and colleagues showed that triptolide causes cell growth arrest in certain cell types.
Requirements to Sell Medication in USA

- Must be approved by FDA (Food and Drug Administration)

- 1906: The original Food and Drugs Act is passed by Congress and signed by President Theodore Roosevelt.

- 1938: The Federal Food, Drug and Cosmetic (FDC) Act is passed by Congress and requires that drugs must be shown to be safe before marketing.

- 1962: The Kefauver-Harris Drug Amendments passed to ensure drug efficacy and greater drug safety; “substantial evidence” necessary from “adequate and well controlled trials” to form the basis for drug approval.

- 1986: Although not an act of Congress, a landmark court decision, Warner-Lambert v. Heckler determined that the effect of a drug must be clinically meaningful (bears heavily on survival, how the patient functions or feels) to establish efficacy.
Types of Clinical Trials

• Interventional: a drug is tested for efficacy and safety
• Observational: natural history of a disease and/or complications without intervention
• Genetic or biochemical testing: provide blood or urine samples for DNA and other measurements
• Image analysis: undergo CT or MRI to evaluate disease characteristics/progression
Phase 1 Clinical Trial

- **Phase I** trials are the first step in testing a new approach in people.

- In these studies, researchers evaluate what dose is safe, how a new agent should be given (by mouth, injected into a vein, or injected into the muscle), and how often. Researchers watch closely for any harmful side effects.

- **Phase I** trials usually enroll a small number of patients and take place at only a few locations. The dose of the new therapy or technique is increased a little at a time. The highest dose with an acceptable level of side effects is determined to be appropriate for further testing.

clinicaltrials.gov and www.cancer.gov/CLINICALTRIALS
Phase 1 Clinical Trial

PHASE I STUDIES HAVE THE MOST UNCERTAINTY

RISKS NOT FULLY KNOWN
Phase 2 Clinical Trial

• In **Phase II** trials, the experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

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Phase 3 Clinical Trial

• In Phase III trials, the experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.

• Phase III trials compare a new agent or intervention (or new use of a standard one) with the current standard therapy.

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Phase 4 Clinical Trial

- In **Phase IV** trials, post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

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PHASES OF DRUG DEVELOPMENT FOR PROMISING COMPOUNDS

- Preclinical Research: 4.5 years
- Preclinical Development
- Pivotal Trials*: 7 years
- Clinical Research*: 1.5 years
- Post-Approval Studies*: 
- Regulatory Review

Average development time: 13 years
Average cost: $500-1000 million
*Studies in humans

PKD Progress February, 2008
Benefits of Participating in a Clinical Trial

• **Early access** to promising new approaches that are often not available outside the clinical trial setting.

• The approach being studied may be more effective than the standard approach.

• Participants receive regular and careful medical attention from a research team that includes doctors and other health professionals.

• Results from the study may help others in the future.

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Possible Risks of Participating in a Clinical Trial

- New drugs or procedures under study are not always better than the standard care to which they are being compared.
- New treatments may have side effects or risks that doctors do not expect or that are worse than those resulting from standard care.
- Participants in randomized trials will not be able to choose the approach they receive.
- Health insurance and managed care providers may not cover all patient care costs in a study.
- Participants may be required to make more visits to the doctor than they would if they were not in the clinical trial.

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Clinical Trials Require Your Participation

• New treatments MUST be tested in humans for safety and effectiveness.
  – Animal testing and computer simulation is not sufficient and does not meet the legal standard required by FDA

• Without your participation, new treatments will NOT be developed!
### ClinicalTrials.gov

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Questions?