

Your Patient and HALT PKD

A description of HALT PKD has been included within this brochure to provide you with a general overview of the study.

As the study moves forward, it may be necessary for HALT PKD to call on you from time to time to request your help with a participant who is under your care. Reasons for which you may be contacted by a Principal Investigator or Study Coordinator include:

- To request relevant medical records, including ultrasounds.
- To request certain lab tests be obtained (at study expense) for safety or follow-up.
- To request follow-up between study visits, if necessary.
- To request your assistance in managing an adverse event.

HALT PKD will inform you of any medically significant abnormal results from laboratory tests and imaging studies if your patient authorizes release of his/her Protected Health Information (PHI).

If you have patients who may be interested in study participation, we invite you to tell them about HALT PKD. To learn more, patients may contact the HALT PKD Project Manager at (314) 362-1318 or visit the HALT PKD website at www.pkd.wustl.edu/pkdtm.

HALT PKD

Participating Clinical Centers

Beth Israel Deaconess Medical Center, Boston, MA
Principal Investigator: Dr. Theodore Steinman
Call (Toll-Free): (866) 650-1815

Cleveland Clinic Foundation, Cleveland, OH
Principal Investigator: Dr. William Braun
Call (Toll-Free): (800) 223-2273, Extension 44680

Emory University, Atlanta, GA
Principal Investigator: Dr. Arlene Chapman
Call: (404) 686-8280

Kansas University Medical Center, Kansas City, KS
Principal Investigator: Dr. Franz Winklhofer
Call: (913) 588-7609

Mayo Clinic, Rochester, MN
Principal Investigator: Dr. Vicente Torres
Call (Toll-Free): (888) 630-2616

Tufts-New England Medical Center, Boston, MA
Principal Investigator: Dr. Ronald Perrone
Call (Toll-Free): (866) 846-2735

University of Colorado Health Sciences Center, Denver, CO
Principal Investigator: Dr. Robert Schrier
Call (Toll-Free): (877) 765-9297

Data Coordinating Center
Washington University, St. Louis, MO
Principal Investigator: Professor J. Philip Miller

Project Manager: Ms. Robin Woltman
(314) 362-1318

www.pkd.wustl.edu/pkdtm

Information for Physicians

HALT PKD

A Clinical Research Study To HALT Progression of Polycystic Kidney Disease



Developed by the
Polycystic Kidney Disease
Treatment Network

Sponsored by
The National Institute of Diabetes &
Digestive & Kidney Diseases (NIDDK)
The National Institutes of Health (NIH)
U.S. Department of Health and
Human Services

HALT PKD—Information for Physicians

HALT PKD is a 4-6 year, multi-center study, funded by NIH, in which participants will be eligible for 1 of 2 studies, depending on their level of kidney function as measured by GFR.

Study A

Preserved Kidney Function (GFR > 60 mL/min/1.73 m²)

- **Purpose:** Evaluate efficacy of dual vs. single blockade of the renin-angiotensin system on kidney cyst growth using a combination of ACE inhibitor (ACE-I) and ARB vs. ACE-I alone and usual (120-130/70-80 mm Hg) vs. low blood pressure control (95-110/60-75 mm Hg). The ARB and control will be masked.
- **Outcome:** Percent change in kidney volume (cyst growth), as measured by MRI at baseline, 2 and 4 years.

Study B

More Advanced Kidney Disease (GFR 30- 60 mL/min/1.73 m²)

- **Purpose:** Evaluate efficacy of multi-level blockade of the renin-angiotensin system using a combination of ACE-I and ARB vs. ACE-I alone on slowing loss of kidney function independent of blood pressure control. The ARB and control will be masked.
- **Outcome:** Time to 50% reduction of baseline eGFR, ESRD, or death.

HALT PKD may ask the primary care physician or nephrologist to obtain a serum creatinine sample (at study expense), on occasion, and forward it to the central laboratory at Cleveland Clinic for analysis.

Study Overview

Participants will take a combination of either Lisinopril (ACE-I) and Telmisartan (ARB) or Lisinopril and placebo, with doses titrated to maintain blood pressure (BP) within the assigned range. If necessary, a diuretic and additional antihypertensive medications will be added to maintain the BP goal. Participants will monitor BP at home, with a Study Coordinator phoning every 2 weeks during titration to discuss BP readings. Dose adjustments will be made according to protocol, based on these BP readings. Subsequent telephone contact will occur every 3 months. Follow-up visits at the study site will occur twice in the 1st year, then every 6 months until the study ends. Serum potassium and creatinine will be measured up to 4 times during the 8-week titration period and will be measured at each follow-up visit.

Safety

HALT PKD requires additional safety testing (serum creatinine and potassium) for participants who meet either of the criteria below .

- Hyperkalemia—High normal or potassium level ≥ 5.6 .
- GFR <30 mL/min/1.73 m²

HALT PKD will notify the primary care physician or nephrologist of any medically significant lab results if the participant has granted authorization for the study to release PHI.

HALT PKD may also ask the primary care physician or nephrologist to obtain the required safety labs, serum creatinine and potassium (at study expense), and forward the results to the study site.

Eligibility Criteria

Inclusion Criteria

1. Diagnosis of ADPKD.
2. Age 15-49 (Study A); Age 18-64 (Study B).
3. GFR >60 mL/min/1.73 m² (Study A).
GFR 30-60 mL/min/1.73 m² (Study B).
4. BP $\geq 130/80$ or receiving treatment for hypertension.
5. Informed Consent.

Exclusion Criteria

1. Pregnant/intention to become pregnant in 4-6 yrs.
2. Documented renal vascular disease.
3. Spot urine albumin-to-creatinine ratio of ≥ 0.5 (Study A) or ≥ 1.0 (Study B) and/or findings suggestive of kidney disease other than ADPKD.
4. Diabetes requiring insulin or oral hypoglycemic agents / fasting serum glucose of ≥ 126 mg/dl / random non-fasting glucose of ≥ 200 mg/dl.
5. Serum potassium >5.5 mEq/L for participants currently on ACE-I or ARB; >5.0 mEq/L for participants *not* currently on ACE-I or ARB.
6. History of angioneurotic edema or other absolute contraindication for ACE-I or ARB. Intolerable cough associated with ACE-I is defined as a cough developing within six months of initiation of ACE-I in the absence of other causes and resolving upon discontinuation of the ACE-I.
7. Absolute indication (but not hypertension) for β -blocker or calcium channel blocker therapy.
8. Systemic illness necessitating NSAIDs, immunosuppressant or immunomodulatory medications.
9. Systemic illness with renal involvement.
10. Hospitalized for acute illness in past 2 months.
11. Life expectancy <2 years.
12. History of non-compliance.
13. Unclipped cerebral aneurysm ≥ 7 mm diameter.
14. Creatine supplements within 3 months of screening visit.
15. Congenital absence of a kidney (also total nephrectomy for Study B).
16. Known allergy to sorbitol or sodium polystyrene sulfonate.
17. Exclusions specific to MR imaging (Study A).