Dear Colleague,

At UPMC Presbyterian and Children's Hospital of Pittsburgh of UPMC, we're conducting a new clinical drug trial, supported by the National Institutes of Health, that involves the study of carbamazepine (Tegretol*) and its use in the treatment of alpha-1 antitrypsin (AT) deficiency, or ATD. As you may be aware, our laboratory research indicates that carbamazepine shows significant promise for reversing and preventing fibrosis from ATD. In mice, this drug promotes autophagy, enhancing clearance of accumulated and toxic ATZ protein, which leads to a reduction in fibrosis. These findings were published in an article in the July 9, 2010, edition of Science.

To further investigate the drug's efficacy, our clinical trial examines the effect carbamazepine has on patients diagnosed with AT deficiency. Participation in the trial will be one year and we are currently accepting qualified participants who:

- ✓ are at least 14 years of age and less than 80 years of age
- ✓ have AT deficiency confirmed by ZZ or SZ phenotype
- ✓ have serum levels of AT less than 83 mg/dl
- ✓ have compensated cirrhosis secondary to the confirmed AT deficiency
- ✓ meet other inclusion criteria (available upon request)

How Will The Trial Work?

Those interested in participating in the trial will be screened to ensure they meet all trial criteria. After acceptance into the study, participants will be asked to schedule a baseline visit where a complete medical history will be taken, a physical examination performed, and blood tests obtained to assess liver function. After agreeing to the gathering of baseline data that will include hepatic venous pressure gradient (HVPG) measurements and transvenous liver biopsies, participants will be prescribed either a placebo or Tegretol-XR 1200 mg/day (400 mg and 200 mg extended-release tablets taken twice daily) for 12 months. Clinical and biomedical follow-up will help assess tolerability of Tegretol in trial participants. After 12 months of drug therapy and medical monitoring, HVPG and transvenous liver biopsies will be repeated. Based on this data, researchers will make a formal assessment of the effects of Tegretol on ATZ load and fibrosis.

Where Can I Learn More?

A description of the study is found at www.chp.edu/liverstudy. This web page includes a link to a Toolkit for Physicians with information that will help you explain the program to parents as well as additional information about ATD. You may also call 1-855-428-2281 or e-mail us at liverstudy@chp.edu for additional information or to refer a patient.

Thank you for your support of our research initiatives.

Sincerely,

Robert H. Squires, MD
Principal Investigator
Division of Pediatric Gastroenterology
Children's Hospital of Pittsburgh of UPMC
Professor of Pediatrics
University of Pittsburgh School of Medicine

Kapil B. Chopra, MD
Director
UPMC Center for Liver Diseases
Associate Professor of Medicine
University of Pittsburgh School of Medicine

*Tegretol is a registered trademark of Novartis Pharmaceuticals, Inc.