CHAPTER 1. OVERVIEW

1.1 Summary of Study

The overall hypothesis is that therapy with corticosteroids following portoenterostomy will improve bile drainage and long-term outcome in infants with biliary atresia. This hypothesis will be tested by a multi-center prospective, randomized, double-blinded, placebo-controlled trial. Subjects will be recruited from patients enrolled in the Childhood Liver Disease Research and Education Network (ChiLDREN) prospective observational database (PROBE) study, who undergo portoenterostomy for biliary atresia. The Principal Investigator (PI) or Clinical Research Coordinator (CRC) will approach the subject's parent(s) or legal guardian(s) and discuss the study design, benefits and possible risks with the family.

After Institutional Review Board (IRB)-approved written consent is obtained from the subject's parent(s) or legal guardian(s), the CRC will:

- Complete the Eligibility Form
- Randomize the subject to 13 weeks of treatment with placebo or corticosteroids. (The research team will be blinded to the treatment. The randomization scheme will be prepared by the University of Michigan (UM) Data Coordinating Center (DCC) and implemented by the research pharmacist.)
- Collect clinical and biochemical data at 2 weeks after portoenterostomy, at 1, 2, 3, and 6 months after portoenterostomy, and at 12, 18, and 24 months of age.

All subjects will receive standard clinical care that is routinely used for all infants with biliary atresia, which will include nutritional support and medications unrelated to this trial. This routine clinical care will not be modified due to participation in this study. One important feature of this clinical trial is that subjects will receive standard clinical care at ChiLDREN study sites, in addition to the care related to enrollment in the trial.

The trial will specifically require:

1) Randomization to receive either corticosteroids or placebo.
2) Treatment with ranitidine during the duration of study drug/placebo
3) Outpatient visit at 2 weeks after portoenterostomy
4) Serum concentration of electrolytes, glucose, bile acids, and Proteins Induced by Vitamin K Antagonism or Absence (PIVKA)-II.
5) Developmental assessment
6) Health-Related Quality of Life (HRQOL) inventory
7) Evaluation of serum antibody titers to vaccines.
8) Ophthalmology exam / cataract screening.
9) Assessment of vitamin levels.

All other outpatient visits and laboratory studies are routinely performed as part of standard clinical care of infants with biliary atresia.