PFIC PC-CER Targets

Background – Using data collected through the Treatment Experience App (TEA), IMPACT focus groups, and surveys, participants generated a comprehensive list of treatment-related questions. These questions were then refined to identify those that could be addressed in a patient-centered comparative effectiveness research (PC-CER) study (see Table 1 below). The final set of questions is categorized into four key areas: Medications, Surgeries, Nutrition, and Delivery of Care & Other Support. Participants also identified key outcomes to assess treatment effectiveness in the proposed questions, categorized into two types: patient-reported and clinical (see Table 2 below).

Table 1. Treatment Questions

TOPIC	QUESTIONS
Medications	<u>IBAT-related medications</u> • What is the comparative effectiveness of rifampin, ursodiol, and cholestyramine in reducing itch? • Among PFIC patients who respond well to IBAT therapy and those with a partial response, what is the comparative impact of continuing versus discontinuing non-IBAT medications on itch, quality of life, sleep, fatigue, and overall medication burden? • Among PFIC patients undergoing diversion surgery, how do growth, nutrition, sleep, and itch outcomes compare between those receiving surgery alone and those receiving surgery combined with IBAT therapy? <u>Non-IBAT medications</u> • What is the best way to manage the psychological effects of PFIC on patients and families during any stage of the disease? • How does the mental and the general health of PFIC patients receiving psychological intervention compare with those who receive none? • Among PFIC patients with and without IBAT therapy, how does exposure to hot versus cold temperatures impact itch severity and quality of life? • What are the comparative effects of wearing cotton, silk, or bamboo clothing on itch severity, sleep quality, and overall quality of life? • What is the comparative effectiveness of prescription-strength Benadryl versus Atarax in improving sleep and quality of life? <u>Liver transplant & post-transplant medications</u> • Which is more effective at reducing post-transplant pruritus in patients with recurrent BSEP: IBAT inhibitors, Plasmapheresis, rituximab, MARS, or a combination of these therapies? • What is the comparative effectiveness of loperamide, Imodium, IBAT inhibitors, external and internal biliary diversion surgery in reducing diarrhea and improving quality of life post-transplant?

Surgeries	<u>Biliary diversion</u> • What is the comparative effectiveness of internal versus external biliary diversion surgery for native liver survival, itch reduction, and quality of life, and how do these outcomes vary across PFIC subtypes and genetic mutations? • What is the comparative effectiveness of biliary diversion surgery and liver transplant for long-term patient survival, itch reduction, quality of life, risk of cancer, financial burden, and how do these outcomes vary across PFIC subtypes and genetic mutations? <u>Surgeries and IBATs</u> • Which delays the need for liver transplant longer: diversion surgery or IBAT inhibitors? • How does the financial burden of surgical biliary diversion or liver transplant compare to the financial burden of being prescribed an IBAT inhibitor long-term? <u>Liver transplant</u> • What is the comparative effectiveness of different timing strategies for liver transplantation in improving outcomes such as survival, quality of life, and symptom management for individuals with PFIC? • How does a live donor liver transplant compare to a deceased donor liver transplant when it comes to care, longevity, and quality of life after transplant? • How do growth and quality of life compare pre- and post- liver transplant?
Nutrition	<u>Vitamins & Supplements</u> • What types of OTC supplements best support growth and development? • How do aggressive nutritional treatments (such as NG tubes or TPN) compare to more passive approaches (like oral formulas) in terms of tolerability, as well as their impact on weight, growth, and quality of life? • How does regular versus infrequent monitoring of vitamin levels impact health and quality of life outcomes related to vitamin deficiencies? <u>Diet</u> • Which is better: formula or blended food? • How does an MCT-enhanced diet impact growth versus a non- MCT enhanced diet? • How does a diet high in processed foods, sugars, fats, and starches compare with one containing fewer of these elements in terms of its impact on pruritus, gastrointestinal symptoms, quality of life, and liver health?
Delivery of care, & other support	<u>Delivery of care</u> • What is the comparative effectiveness of combining hormonal pattern tracking, such as menstrual cycles, with standard itch assessment methods versus using standard itch assessment methods alone in understanding and managing fluctuations in itch severity and sleep disturbances in post-pubertal female PFIC and BRIC patients? • What is the comparative effectiveness of pain management intervention (e.g., EMLA cream or gas protocol for needle insertion) versus no pain management intervention in improving patients' mental health? • What is the comparative effectiveness of having a dietician in the care team versus no dietician in improving nutrition and quality of life outcomes for PFIC patients?

	Other support • What is the best way to make the process of insurance approvals for medications easier and faster? • What is the best way to educate my providers and specialists about PFIC? • What is the best way to educate my child's school personnel about PFIC? • What is the best way to improve the transition from pediatric to adult care? • What is the best supplemental insurance to help cover costs associated with PFIC?

Note: IBAT = Ileal Bile Acid Transporter. OTC = Over the Counter. NG = Nasogastric. TPN = Total Parenteral Nutrition. MCT = Medium Chain Triglyceride. EMLA = Eutectic Mixture of Local Anesthetics.

Table 2. PFIC Treatment Outcomes to Measure

OUTCOME TYPE	OUTCOMES
Patient-Reported	Medications-specific • Level of itch, skin health, sleep quality, level of pain, level of fatigue, frequency and severity of diarrhea, frequency and severity of episodes Surgeries-specific • Level of itch, level of abdominal pain/discomfort, level of social acceptance (e.g., concerning ostomy bags), frequency and severity of diarrhea, effect on toilet training Nutrition-specific • Palatability (e.g. taste, pill size, and consumption of required doses), burden of medication management (e.g. number of medications, manner of administration, and yes/no need for refrigeration), level of risk of vitamin deficiencies and associated symptoms, level of risk of vitamin toxicity Cross-intervention • Patient quality of life, quality of life for caregivers/family/siblings, mental health (anxiety/depression/irritability), focus and school performance, ability to enjoy major life events, ability to play and swim, ability to do outdoor activities in the summer heat, quality of REM sleep, level of experienced bullying and social stigma associated with growth delays Care Delivery & Support-specific • Number of workdays missed for care, financial burden of the disease and treatments, impact of delayed insurance approvals on quality of life, impact of switching insurance companies on treatment access, ease of acquiring compounded medications, trust in provider/healthcare system, testing for cancers, anxiety and fear related to flare-ups, medical procedures (e.g., blood draws), and disease progression
Clinical	Medications-specific • Effects on disease progression Surgeries-specific • Native liver survival, reduced post-transplant complications

	<u>Nutrition-specific</u> • Vitamin levels, weight change, growth (height) change, change in strength, effects on hearing loss

Note: Participants identified key patient-reported and clinical outcomes within and across the four categories of treatments/interventions from Table 2 (medications, surgeries, nutrition, care delivery and other support).