PSC and PBC Patient Meeting

January 21, 2017
University of California Davis
Genome and Biomedical Sciences Building
Agenda

• PSC and PBC Basics

• Current Treatments for PBC

• Current Treatments for PSC

• Drugs in Clinical Trials for PSC and PBC
Primary ________ Cholangitis

- **Primary** = No underlying cause
- **Biliary** = Involving the bile ducts
- **Cholangitis** = Inflammation of the bile ducts
- **Cirrhosis** = end-stage of liver disease

- **Primary** = No underlying cause
- **Sclerosing** = hardening of tissue
- **Cholangitis** = Inflammation of the bile ducts
PSC and PBC Basics

• PSC and PBC are autoimmune diseases that attack the bile ducts

• PBC targets the small bile ducts

• PSC targets the large bile ducts
PSC and PBC Basics

**PSC**
- Male > Female
- 3 > 2

**PBC**
- Female > Male
- 9 > 1

**Inflammatory Bowel Disease**
- Healthy
- Crohn's disease
- Ulcerative colitis

**Sjogren's Syndrome**
- Dry eyes, damage to eye surface
- Dry mouth, increased tooth decay

**AMA**
PBC Clinical Endpoints

- AMA
- Loss of Tolerance to PDC-E2
- Elevated ALP
  - Immune-mediated cholangitis
- Cholestasis
  - Ductopenia
- Portal Hypertension
  - Cirrhosis
- Variceal Bleeding
- Impaired Quality of Life
  - Fatigue
  - Pruritus
- Liver-related Death/Liver Transplantation
NATURAL HISTORY OF PSC

Colitis

Biliary Inflammation

Biliary Fibrosis

Portal Hypertension

Variceal Bleeding

Liver-related Death/Liver Transplantation

Pre-Clinical PSC

• Elevated ALP

• Abnormal Cholangiogram

• Cirrhosis

Competing Outcomes

• Cholangiocarcinoma
• Gallbladder cancer
• Colon cancer
• Hepatocellular carcinoma
• Bacterial cholangitis
• Colitis flare/Pouchitis
• Diabetes/CVD
PBC: Biochemical Response to Urso at 1 Year

• Lack of Complete Biochemical Response Predicts Disease Progression

Incomplete Responders are more to be:
• Younger Women
• Men
• Hispanic

Obeticholic Acid in PBC (POISE)

*Responders were defined as patients with ALP <1.67xULN, ≥15% ALP reduction, and normal bilirubin
PSC: Biochemical Response to Urso

- Normal Alkaline Phosphatase Predicts Better Prognosis

Normalization can be spontaneous or from Urso

Urso and Drugs Targeting Bile Acids
# Drug Pipeline for PBC

<table>
<thead>
<tr>
<th>Bile Acid Based Therapies</th>
<th>Phase of Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS-9674 (Gilead)</td>
<td>2</td>
</tr>
<tr>
<td>NGM282 (NGM Biopharmaceuticals)</td>
<td>2</td>
</tr>
<tr>
<td>LJN 452 (Novartis Pharmaceuticals)</td>
<td>2</td>
</tr>
<tr>
<td>MBX-8025 (CymaBay)</td>
<td>2</td>
</tr>
<tr>
<td>Intestinal Apical Sodium Bile Acid Transport (iASBT) inhibitors</td>
<td></td>
</tr>
<tr>
<td>SHP625 (LUM001; Shire) <em>Negative Results</em></td>
<td>2</td>
</tr>
<tr>
<td>GSK2330672 (GlaxoSmithKline)</td>
<td>2</td>
</tr>
<tr>
<td>A4250 (Albireo Pharma)</td>
<td>2</td>
</tr>
<tr>
<td>Immune-based Therapies</td>
<td></td>
</tr>
<tr>
<td>Budesonide (Falk)</td>
<td>2</td>
</tr>
<tr>
<td>Abatacept (BMS)</td>
<td>2</td>
</tr>
<tr>
<td>FFP104 (FFPharma)</td>
<td>2</td>
</tr>
<tr>
<td>Ustekinumab (Janssen) – <em>Negative Results</em></td>
<td>2</td>
</tr>
</tbody>
</table>
# Drug Pipeline for PSC

<table>
<thead>
<tr>
<th>Bile Acid Based Therapies</th>
<th>Phase of Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCA (Intercept) <em>Enrollment Completed</em></td>
<td>2</td>
</tr>
<tr>
<td>GS-9674 (Gilead)</td>
<td>2</td>
</tr>
<tr>
<td>NGM282 (NGM Biopharmaceuticals)</td>
<td>2</td>
</tr>
<tr>
<td>Nor-UDCA (Falk) <em>Positive Results</em></td>
<td>2</td>
</tr>
<tr>
<td><strong>Intestinal Apical Sodium Bile Acid Transport (iASBT) inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>SHP625 (LUM001; Shire) <em>Negative Results</em></td>
<td>2</td>
</tr>
<tr>
<td><strong>Anti-Fibrotic</strong></td>
<td></td>
</tr>
<tr>
<td>Simtuzimab (Gilead) <em>Enrollment Completed</em></td>
<td>2</td>
</tr>
<tr>
<td><strong>Immune-based Therapies</strong></td>
<td></td>
</tr>
<tr>
<td>Cenicriviroc (Tobira)</td>
<td>2</td>
</tr>
<tr>
<td>Vancomycin (Stanford)</td>
<td>2</td>
</tr>
<tr>
<td>FMT (Mass General)</td>
<td>2</td>
</tr>
</tbody>
</table>
Opportunities for PSC and PBC Clinical Trials

• Investigator
  Christopher L. Bowlus, MD, Division of Gastroenterology and Hepatology, UC Davis Medical Center

• Purpose of the research
  Development of New Therapies for PSC and PBC

• Participation benefits
  No-cost health examination, lab tests

• Location and Contact
  2000 Stockton Blvd, Sacramento, CA 95817
  Sandeep Dhaliwal 916-734-8985