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747-207 AESOP Overview and Inclusion/Exclusion Criteria

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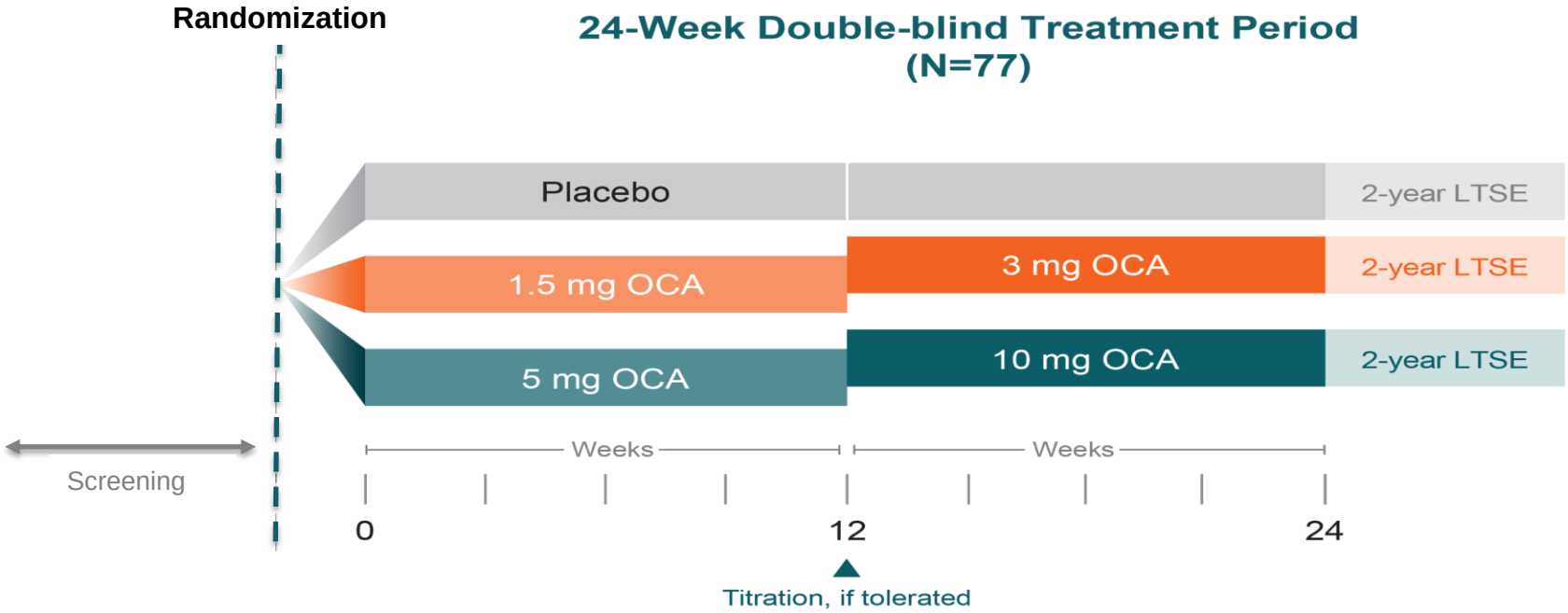
AESOP: A Phase 2 Randomized, Placebo-Controlled Trial, Dose-Finding Clinical Trial Evaluating the Efficacy and Safety of Obeticholic Acid in Patients with PSC



clinicaltrials.gov: NCT02177136

Primary and Secondary Measures

- Primary
  - Evaluate the effects of obeticholic acid (OCA) on ALP in patients with PSC
- Secondary
  - To evaluate the effects of OCA at week 24 on:
    - Hepatic biochemistry and indices of function
    - Hepatic fibrosis
    - GI inflammation and disease
    - FXR activity
    - Inflammatory Bowel Disease (IBD)
    - Exposure response of total OCA (and its conjugates) to biomarkers
    - Long term safety and efficacy
    - Disease symptoms
    - PK of OCA and other bile acids

https://clinicaltrials.gov/ct2/show/NCT02177136?term=NCT02177136&rank=1. Accessed April 3, 2018

Key Inclusion/Exclusion Criteria: PSC Diagnosis and General Considerations

Inclusion

- Diagnosis of PSC based on cholangiography
- Written informed consent and agree to comply with the trial protocol
- Age 18 to 75

Exclusion

- Secondary causes of sclerosing cholangitis
- IgG4 >4x ULN
- Small duct disease in absence of large duct disease
- History of other chronic liver diseases e.g., PBC, NASH, hepatitis B/C
- Known Gilbert's syndrome or history of elevations in unconjugated bilirubin or unconjugated bilirubin >ULN at Screening

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Key Inclusion/Exclusion Criteria: IBD

Inclusion

- For subjects with concomitant IBD:
  a) Colonoscopy (if subject has a colon) or other appropriate endoscopic procedure within 12 months of Day 0 confirming no dysplasia or colorectal cancer
  b) Subjects with Crohn's Disease must be in remission as defined by a CDAI <150.
  c) Subjects with UC must either be in remission or have mild disease.*

Exclusion

- IBD flare during Screening (up to and including Day 0), where “flare” is defined as follows:
  - UC flare: partial Mayo Score ≥5, and
  - CD flare: CDAI ≥250

*Remission is defined as a partial Mayo score of ≤2 with no individual sub-score exceeding 1. Mild disease is defined as a partial Mayo score ≤3 with no individual sub-score exceeding 1 point.

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Key Inclusion/Exclusion Criteria: Concomitant Medications

Inclusion

- For subjects using UDCA, the dose must have been stable for ≥ 3 months prior to, and including, Day 0 and must not have exceeded 20 mg/kg/day.*
- Subjects being administered biologic treatments, immunosuppressants, systemic corticosteroids, or statins, must have been on a stable dose prior to and throughout the trial.

Exclusion

- Current or recent history of pruritus requiring systemic or enteral treatment
- Administration of antibiotics is prohibited ≤1 month of Day 0 (unless subject is on a stable prophylaxis dose).
- Administration of the following is prohibited ≤ 6 months of Day 0 and throughout the trial: fenofibrate or other fibrates and potentially hepatotoxic medications.

*Patients using UDCA were capped at no more than 50% of the cohort.

https://clinicaltrials.gov/ct2/show/NCT02177136?term=NCT02177136&rank=1. Accessed April 3, 2018

Key Inclusion/Exclusion Criteria: Disease Severity/Study Endpoint

Inclusion

- ALP ≥2x ULN at Screening
- Total bilirubin < 2.5x ULN at Screening

Exclusion

- Presence of clinical complications of chronic liver disease or clinically significant hepatic decompensation
- Colonic dysplasia within ≤ 5 years prior to Day 0
- History of small bowel resection
- Known/suspected acute cholangitis in 3 months prior to Day 0

https://clinicaltrials.gov/ct2/show/NCT02177136?term=NCT02177136&rank=1. Accessed April 3, 2018

Key Inclusion/Exclusion Criteria: Disease Severity/Study Endpoint, continued

Exclusion

- Current clinical evidence of dominant strictures that are considered clinically relevant in the opinion of the Investigator or current biliary stent at Screening
- Current cholecystitis or evidence of current biliary obstruction due to gallstones. Asymptomatic gallstones that are not considered a safety risk in the opinion of the Investigator might be acceptable subject to discussion and agreement with the Medical Monitor.

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