U.S. FOOD & DRUG ADMINISTRATION

Regulatory Update
Primary Sclerosing Cholangitis

Y. Veronica Pei, MD, MEd, MPH

PSC Forum

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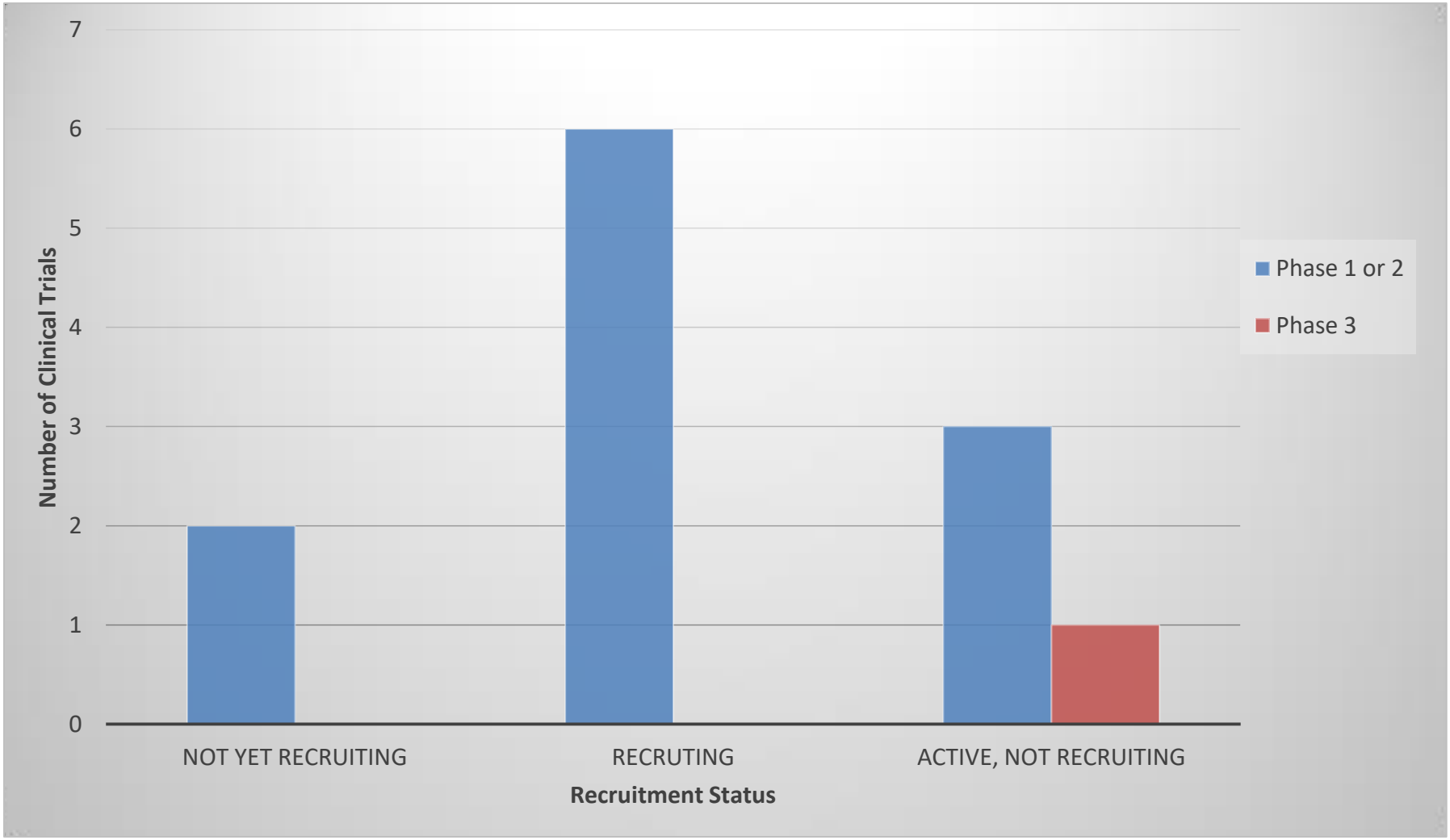
Disclaimer

- The views and opinions expressed here are my own and do not represent official FDA position.

- I have nothing to disclose

Current U.S. Drug/Biologic Interventional Clinical Trials for PSC (April 2018)



https://clinicaltrials.gov/ct2/home; Accessed on April 4, 2018

	Intervention	Phase	PSC Population	Primary Outcome/Endpoint(s)*
Recruiting	Drug: DUR-928	2	Adults (18-80 yr) N ≈ 40	% change ALP after 4 weeks
	Drug: HTD 1801	2	Adults (18-75 yr) N ≈ 90	Δ ALP after 6 weeks
	Drug: Curcumin	1/2	Adults (18-75 yr) N ≈ 15	40% Reduction in ALP after 12 weeks ALP <1.5 × ULN
	Drug: BTT1023	2	Adults (18-75 yr) N ≈ 41	↓ ALP after 99 days
	Drug: Vancomycin	1	Adults & children ≤ 40 yr N ≈ 200	Benefit (blood tests, imaging studies and/or liver biopsy changes) after 3 months
	Drug: Mitomycin	2	≥18 yr N ≈ 130	Therapeutic Effect on Disease Prognosis as Determined by the Mayo Natural History Model for PBC at 2 years
Active Not Recruiting	Drug: Vancomycin	3	≥1 yr N ≈ 40	Benefit (blood tests, imaging studies and/or liver biopsy changes) after 3 months
	Drug: GS-9674	2	Adults (18-75 yr) N ≈ 52	Safety and tolerability after 12 weeks
	Drug: OCA	2	Adults (18-75 yr) N ≈ 77	Δ ALP after 24 weeks
	Biologic: Fecal Microbiota	1/2	Adults (≥18 yr) N≈10	Improvement in serum alkaline phosphatase, total bilirubin, alanine aminotransferase (ALT), or aspartate aminotransferase (AST) by 50 % or greater after 12 weeks
Not Yet Recruiting	Drug: Hymecromone	1/2	Adults (≥18 yr) N ≈ 10	Safety and tolerability (6 months on treatment and 6 months post treatment)
	Biologic: Orbcel	1/2	Adults (18-70 yr) N ≈ 56	% change and duration of change in ALP after 56 days

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Types of Endpoints

- Clinical Benefit - Regular Approval
  - How patients feels, functions or survives
- Validated Surrogate – Regular Approval
  - Validated by evidence based justification (e.g., randomized controlled clinical trials) that it can be relied upon to predict, or correlate with clinical benefit
- Surrogate – Accelerated Approval
  - Reasonably likely to predict clinical benefit
  - Determination made on a case-by-case basis by the Agency
  - Requires confirmatory trial(s) that verifies clinical benefit (ongoing at the time of approval)

Surrogate Endpoint For PSC

- There is no **single** biomarker that is a clear standalone candidate surrogate that is reasonably likely to predict clinical benefit at this time.

- Choice of surrogate endpoint should depend on the mechanism of action.

- Consideration should be given to developing a composite of multiple biomarkers.


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