



## **PSC Forum 9**

Thursday, November 6, 2025

National Union Building  
918 I Street NW, Washington, DC 20004

### **PSC Forum Acute Cholangitis Working Group Update**

# **Clinical Definition of Acute Cholangitis**

**Michael Trauner, MD**

Div. of Gastroenterology & Hepatology  
Dept. of Internal Medicine III





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# **Clinical Definition of Acute Cholangitis**

**Chris Bowlus, Cynthia Levy, David Assis, Kris Kowdley,  
Michael Trauner**

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# Faculty Disclosure

I herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments, and anything else which could potentially be viewed as a conflict of interest:

## Advisor

Abbvie, Albireo, Agomab, Boehringer Ingelheim, Chemomab, Falk, Gilead, Genfit, Hightide, Intercept, Ipsen, Janssen, Mirum, Novartis, Pliant, ProQR Therapeutics, Rectify

## Grants / research support

Alnylam, Cymabay, Falk, Genentech, Gilead, Intercept, UltraGenyx

## Speakers bureau

Albireo, Falk Foundation, Gilead, Intercept, Ipsen, Madrigal

## Travel grants

AbbVie, Falk Foundation, Gilead, Intercept, Ipsen, Janssen

## Property rights

Co-inventor (service invention) for patents on medical use of *norUDCA* (filed by the Medical Universities of Graz and Vienna)



# Aims of the Acute Cholangitis working group

- Clear definition and grading system for acute cholangitis in PSC
- Establish acute cholangitis as a recognized endpoint in clinical trials
- Understand the impact of acute cholangitis on patient outcomes



# Acute Cholangitis

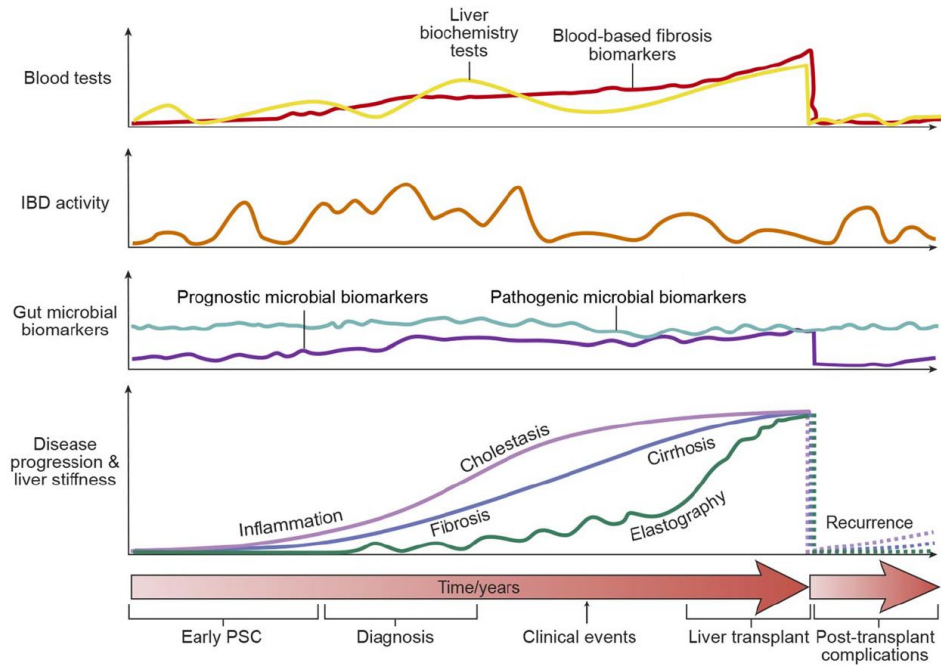
- Bacterial cholangitis usually occurs in patients with a relevant/high-grade/dominant biliary strictures
- Facts to consider
  - Relevant strictures develop in ~50% of people with PSC over time
  - Acute cholangitis may be the first presentation of PSC in up to 5% of cases
  - **Recent phase 3 studies** showed a rather **low rate of cholangitis (~6-7%)** over 96 wks. despite a higher rate of pre-existing dominant/high grade (not all relevant...) strictures (~25%)

**SIM:** 20% at least one PSC-related clinical event (96 wks.)

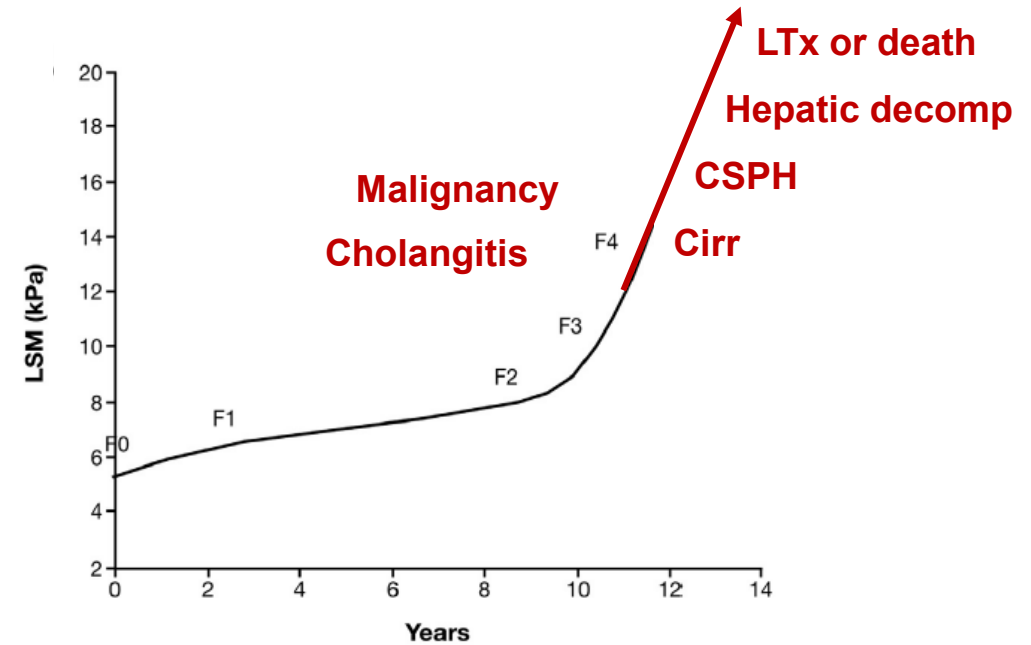
- **Mostly cholangitis (13%)**
- 9% hepatic decompensation
- 1% developed cholangiocarcinoma



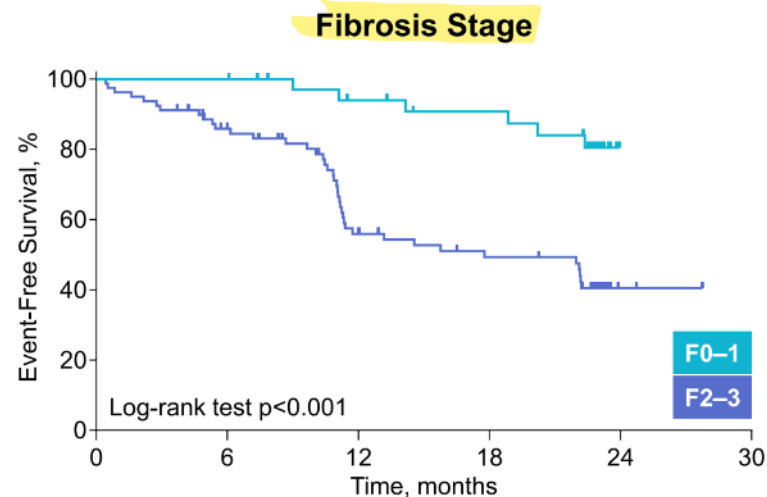
# Disease Course & Clinical Endpoints in PSC



Karlsen et al., *Hepatology* 2024



Corpechot et al., *Gastroenterology* 2014



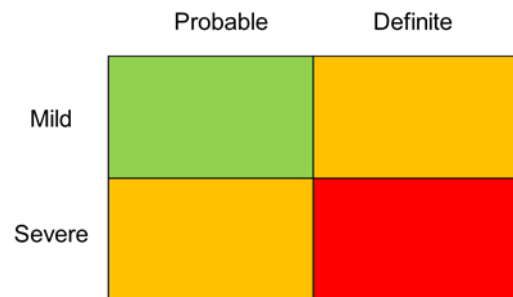
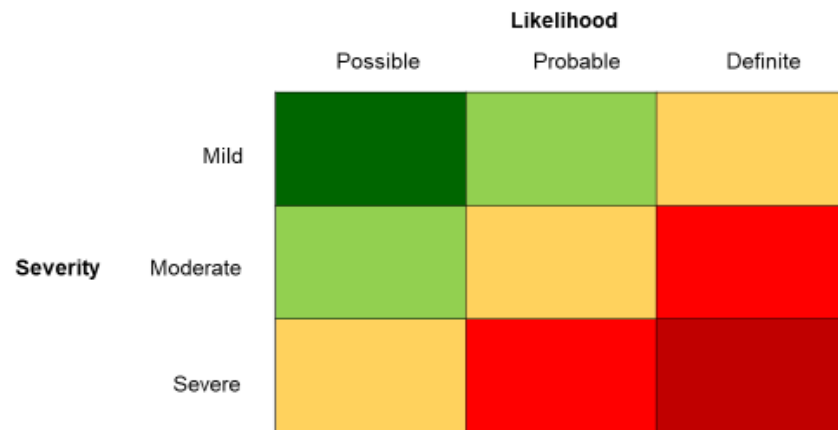
Trauner et al., *BMC Gastro* 2023



# Defining acute cholangitis

Last years' discussion (considering severity and likelihood)

## Heatmap of acute cholangitis



## Defining severity of acute cholangitis

GRADE	Definition
Mild	Oral antibiotics
Moderate	iv antibiotics (more than 1 day)
Severe	Invasive procedures: endoscopic, radiologic, or surgical intervention Life threatening consequences; hypotension; ICU admission

Suggestions for use of Common Terminology Criteria for Adverse Events (CTCAE) grades

GRADE	Definition
2	Oral antibiotics
3	iv antibiotics; endoscopic, radiologic, or surgical intervention
4	Life threatening consequences; hypotension; ICU admission
5	Death

Discussed controversially – perceived as too complicated  
Perhaps the way to go in studies focusing on cholangitis?



# Defining acute cholangitis

New attempt to keep this simple and clinically practical

- Pus in the bile duct (even this may be argued as being subjective)
- Positive bile culture with pathogenic (non-skin flora) bacteria
- Bacteremia (positive blood culture) associated with jaundice (or some elevation of Bili or ALP over baseline)
- Fever associated with jaundice (or some elevation of Bili or ALP over baseline)
- RUQ pain with other systemic signs of infection (leukocytosis, elevated CRP, etc)
  
- Additional requirement:
  - Response to antibiotics and/or biliary intervention
  - Absence of another explanation for these
- Adjudication committee highly recommended



# Defining acute cholangitis

**Table 5. Proposed Definition of Acute Cholangitis for use in clinical trials of PSC**

DOMAIN	ELEMENT	VALUE
<b>Symptoms</b>	RUQ pain	New or worsening
	Other abdominal/back pain	New or worsening (in absence of other explanation)
	Pruritus	New or worsening
	Jaundice	New or worsening
	Fatigue	New or worsening
<b>Inflammation</b>	Fever	T > 38°C
	Shaking chills	New
	Leukocytosis	> 12,000/ $\mu$ l
	CRP	> 7.5 mg/L
	PCT	> 2.0 ng/mL
<b>Cholestasis</b>	ALP or GGT	Increase from baseline
	AST or ALT	Increase from baseline (cave DILI)
	Total bilirubin	Increase from baseline
<b>Infection</b>	Blood culture	Positive (absence of other source)
	Bile culture	Positive (pathogenic / no skin flora)
	Pus in bile duct	Visible (confirmed by Giemsa stain?)



# Defining likelihood of acute cholangitis

## Possible Acute Cholangitis

1 Symptom + 1 Inflammation feature

Acceptable definition in  
context of clinical trials

## Probable Acute Cholangitis

1 Symptom + 1 Inflammation + 1 Cholestasis feature

## Definite Acute Cholangitis

1 Symptom + 1 Inflammation + 1 Cholestasis + 1 Infection feature

N.B.: Pus on ERCP allows a definite diagnosis of acute cholangitis as single criterium  
Response to therapy\* required as additional diagnostic criterium

\*alternatively response to ABx could become infection feature



# Back-up/background slides



## Post-Kasai Procedures

- A. Clinical Elements
  - 1. Fever and/or shivering
  - 2. Stool color change
  - 3. New/increasing jaundice
  - 4. Abdominal discomfort
- B. Laboratory and Imaging Elements
  - 1. Inflammatory response (WBC and/or CRP and/or PCT)
  - 2. Increased/increasing transaminases
  - 3. Increased/increasing GGT and/or bilirubin
  - 4. Bile lakes

### **Suspected Cholangitis**

1 Clinical and 1 Lab or Imaging Element

### **Confirmed Cholangitis**

2 Clinical and 2 Lab or Imaging Elements

OR

Suspected cholangitis with positive blood culture





Article

# Cholangitis Definition and Treatment after Kasai Hepatportoenterostomy for Biliary Atresia: A Delphi Process and International Expert Panel

Ana M. Calinescu <sup>1,\*</sup>, Omid Madadi-Sanjani <sup>2,†</sup>, Cara Mack <sup>3</sup>, Richard A. Schreiber <sup>4</sup>, Riccardo Superina <sup>5</sup>, Deirdre Kelly <sup>6,†</sup>, Claus Petersen <sup>2,†</sup> and Barbara E. Wildhaber <sup>1,†</sup>

## A. Clinical elements

- Fever and/or shivering
- Stool color change
- New/increasing jaundice
- Abdominal discomfort\*

## B. Laboratory and imaging elements

- Inflammatory response (WBC and/or CRP and/or PCT)
- Increased/increasing transaminases
- Increased/increasing GGT and/or bilirubin
- Bile lakes

\*Definition for abdominal discomfort: vomiting, poor feeding, irritability

### Suspected Cholangitis\*\*:

- **Definition:** one item in A + one item in B
- **Treatment:** 10 – 14 days

### Confirmed Cholangitis\*\*:

- **Definition:** two items in A + two items in B
- or
- “suspected cholangitis” + positive blood culture
- **Treatment:** 14 – 21 days

Peroral **prophylaxis** of cholangitis: 6 – 12 months

\*\*Cholangitis within 1<sup>st</sup> year after Kasai



## GUIDELINE

# Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos)

**Table 2** TG18/TG13 diagnostic criteria for acute cholangitis [4]

- A. Systemic inflammation
  - A-1. Fever and/or shaking chills
  - A-2. Laboratory data: evidence of inflammatory response
- B. Cholestasis
  - B-1. Jaundice
  - B-2. Laboratory data: abnormal liver function tests
- C. Imaging
  - C-1. Biliary dilatation
  - C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)

**Suspected diagnosis:** one item in A + one item in either B or C

**Definite diagnosis:** one item in A, one item in B and one item in C

## Thresholds:

A-1	Fever		BT >38°C
A-2	Evidence of inflammatory response	WBC count (×1,000/μL) CRP (mg/dL)	<4 or >10 ≥1
B-1	Jaundice		T-Bil ≥2 (mg/dL)
B-2	Abnormal liver function tests	ALP (IU) γGTP (IU) AST (IU) ALT (IU)	>1.5 × STD <sup>a</sup> >1.5 × STD <sup>a</sup> >1.5 × STD <sup>a</sup> >1.5 × STD <sup>a</sup>



# Wannhoff criteria of superimposed bacterial cholangitis

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**Single criterion:** Suppurative cholangitis on ERC

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**Main criteria ( $\geq 1$ ):** Body temperature  $> 38.0^{\circ}\text{C}$

Leukocyte count  $> 12/\text{nL}$  or CRP  $> 75.0 \text{ mg/L}$

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**Minor criteria ( $\geq 2$ ):** Clinical signs of acute cholangitis (e.g., right upper abdominal pain)

Positive bile culture

Increase in the level of ALP or total bilirubin above two times the upper limit of normal

No other focus of infection

