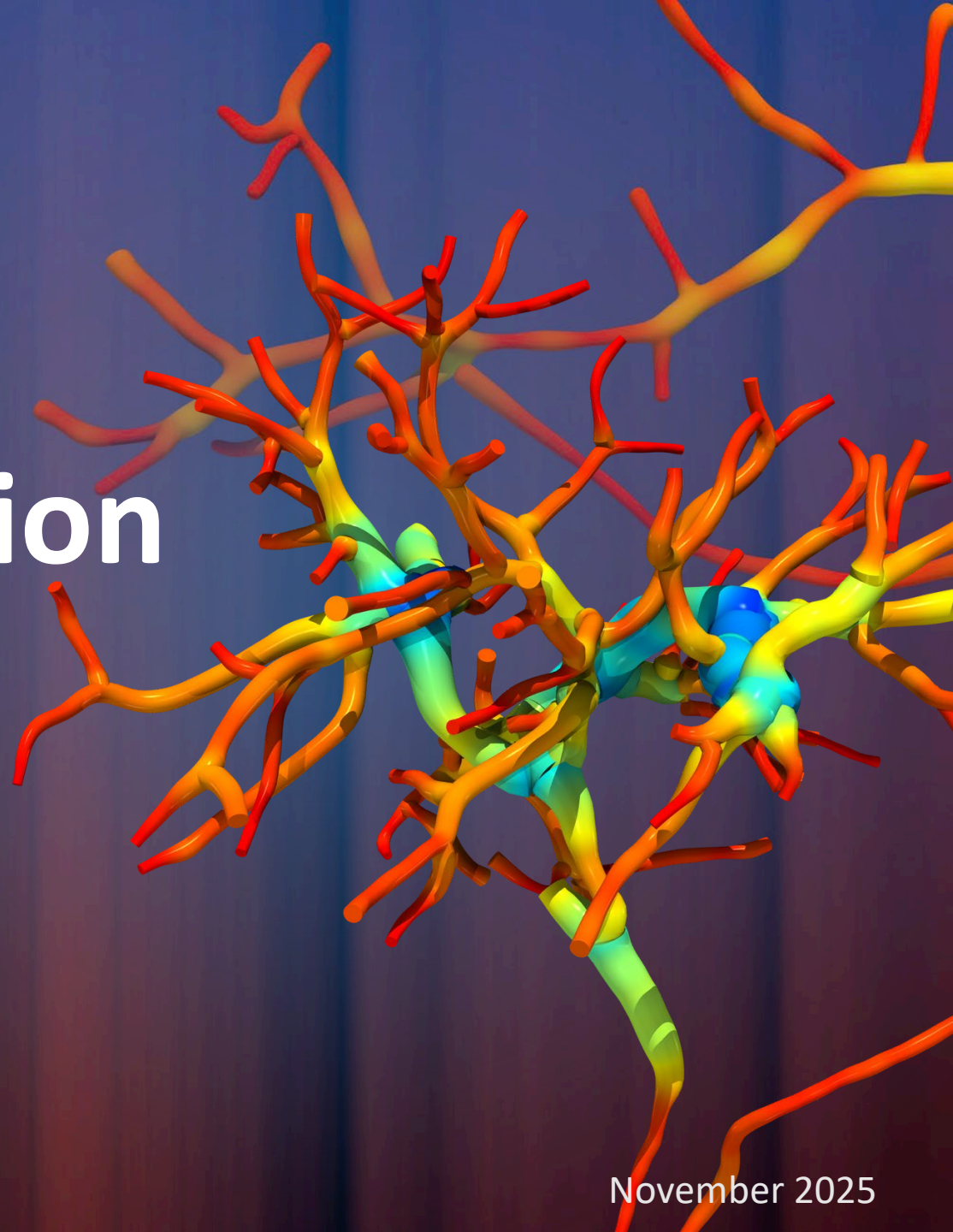
MRCP+ and the biomarker qualification program



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Perspectum

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Disclosure

- Dr. Bowlus is the Principal Investigator for the CHAMPS Study (**CHange Assessment with MRCP+ of PSC Strictures**)

Aims

- Introduction to MRCP+
- Biomarker Qualification program
- Introduction and update on the CHAMPS study
- Current data tally
- Progress with the statistical analysis plan for the BQP

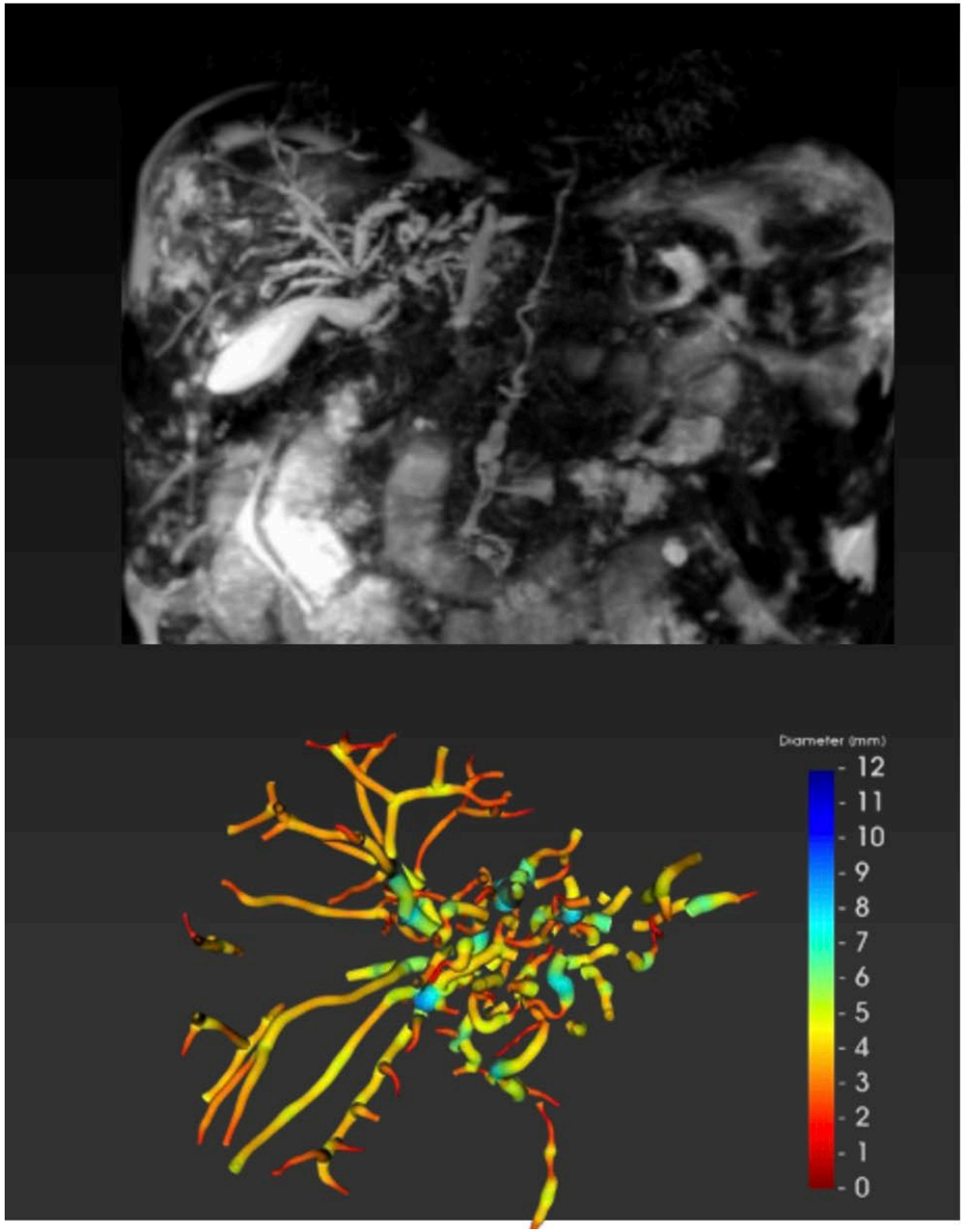
MRCP+

Challenges in monitoring for PSC

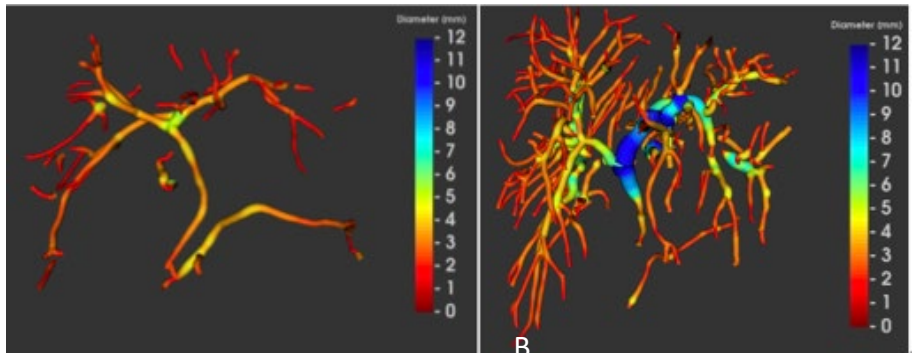
- Blood tests are not reliable
- MRCP interpretation can be variable, subjective and impacted by experience
- Standard MRCP lacks objective assessment when measuring changes over time

Quantitative MRCP

- Enhances standard of care imaging
- Is more reliable than radiological reads*
- Detected changes in biliary anatomy where none were detected by traditional tests*
- Predicted clinical outcomes*

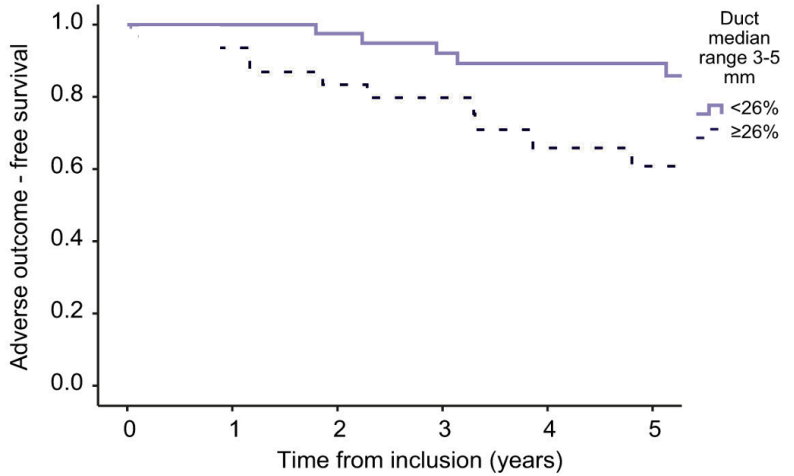


Associations with risk of clinical outcome



MRCP+ results of (A) normal and (B) enlarged biliary tree

MRCP+ metrics enable prediction of adverse-outcome-free survival



MRCP+ metrics associate with increased risk of clinical outcomes:

- Number of bile duct strictures[1]
- Severity of dilations and strictures[2]
- Median diameter of ducts[3]

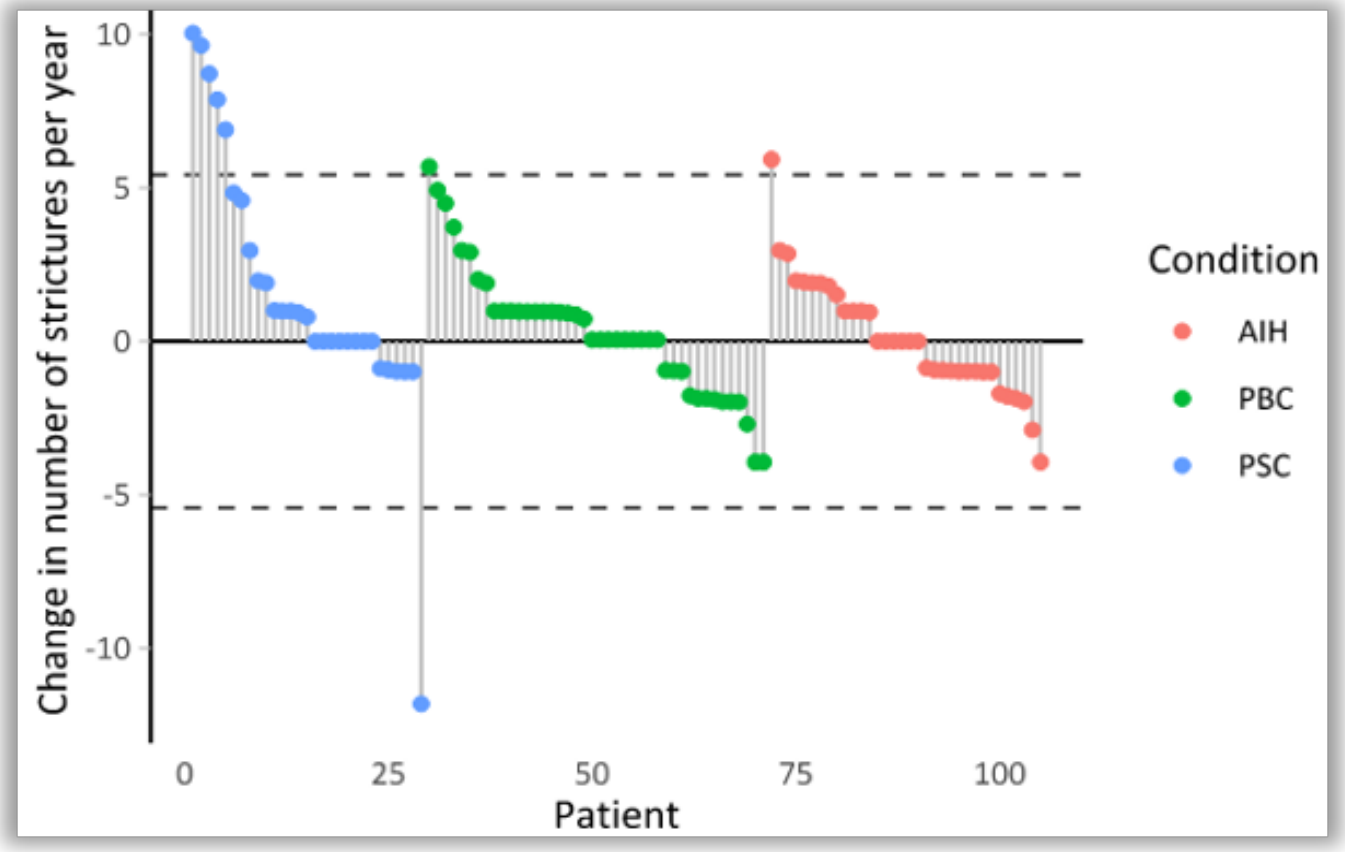
Performance compared to alternative risk scores:

- Number of strictures & spleen length outperformed ANALI score for predicting hepato-biliary complications (c-stat 0.80 v 0.78)[1]
- Duct diameter with bilirubin & AST outperformed Mayo risk score for predicting transplant free survival (HR 5.8 v HR 3.1)[3]

Perspectum

[1] Cristoferi, L., et al. (2022) Dig Liver Dis; [2]Cazzagon, N., et al. (2022). JHEP Reports; [3]Vuppalanchi, R. et al. (2023) JHEP Reports

Enables longitudinal monitoring of biliary changes in patients with PSC



Metrics reported to change over 1 year:

- Number of strictures[1]

Metrics whose change correlates with changes in liver stiffness:

- Number of strictures[2]
- Number of dilatations[2]
- Length of strictures[2]
- Length of dilatations[2]

Perspectum

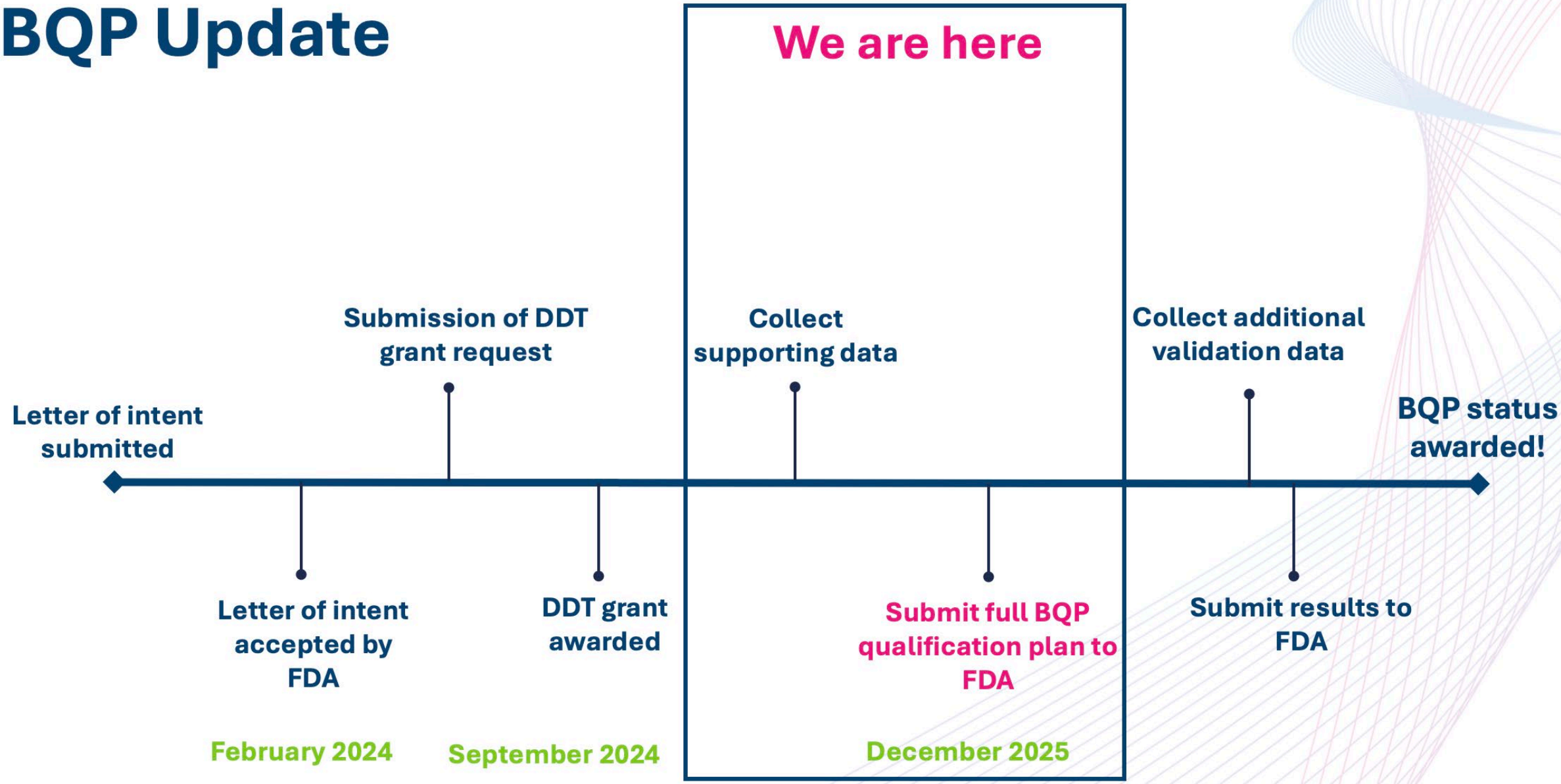
[1]Trivedi et al, (2024). Alimentary pharmacology and therapeutics; [2]Mahalingam et al,. (2023). Abdominal radiology

Letter of intent (LOI)

Context of use

Stricture count as measured by Quantitative Magnetic Resonance Cholangiopancreatography (MRCP) is a non-invasive **monitoring biomarker** to assess disease progression in clinical trials of drugs for **PSC** *(*DDT-BMQ-000146)

BQP Update


We are here
Letter of intent submitted
Submission of DDT grant request
Letter of intent accepted by FDA
February 2024
DDT grant awarded
September 2024
Collect supporting data
Submit full BQP qualification plan to FDA
December 2025
Collect additional validation data
Submit results to FDA
BQP status awarded!

The CHAMPS study

- **Clinically meaningful CHange Assessment with MRCP+ of PSC Strictures**
- FDA funded study to support the BQP qualification plan
- Retrospective data from 150 patients from the CALiD registry
- Eligibility criteria
  - Diagnosis of large duct PSC
  - 2 MRCPs at least 12 months apart. Must have laboratory data within 3 months of the MRCP.
  - Minimum of 6 months from second MRCP to any clinical outcome
- Perspectum and CALiD ensure relevant research protocols and ethical approvals are in place ahead of study initiation.
- Perspectum provides each site MRCP+ reports

CHAMPS study endpoint

Primary Objective:

- To collect clinical data which can be used to determine the prognostic utility of **change in the number of strictures** for predicting clinical outcomes (including cholangitis, requirement to ERCP, cirrhosis, hepatic decompensation, hepatobiliary malignancies, liver transplant or death).

Secondary Objective:

- To assess the prognostic utility of a combination of MRCP+ metrics for predicting clinical outcomes
- To assess the prognostic utility in predicting incidence free transplant free survival
- To assess the agreement between change in MRCP+ and response to ERCP

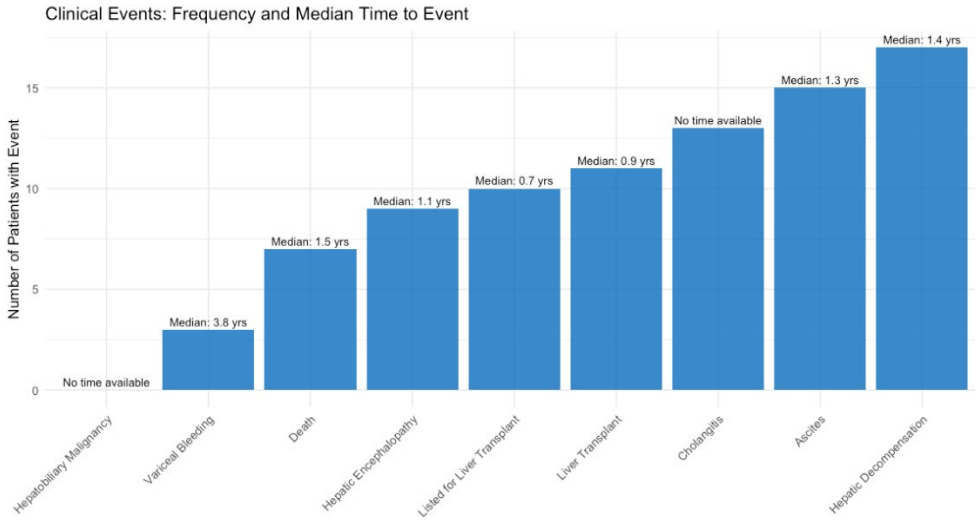
CHAMPS collaborators

- UC Davis - Dr Christopher Bowlus
- Indiana University - Dr Raj Vuppalanchi
- Mass General Hospital - Dr Daniel Pratt
- University of Miami - Dr Cynthia Levy

CHAMPS clinical outcomes

Cohort summary:

- 60 participants
- Median age at diagnosis (IQR): 35.5 years old (27)
- All large duct PSC
- Baseline liver stiffness – MRE (kpa): 3.4
- 63% Male, 37% Female
- 73% White, 15% Black or African American, 8% Asian
- Median no. of ERCP's (Range): 1 (20)
- Cirrhosis - 42%, Ascites – 25%



Median lab values

Scan 1

- Sodium (Na) (mEq/L): 137
- Creatinine: 0.8
- Albumin (g/dL): 3.7
- Alkaline Phosphatase (IU/L): 195
- AST (IU/L): 48.5
- Total Bilirubin (mg/dL): 0.9
- ALT (IU/L): 55.5
- White Blood Cell Count: 6.2
- Hemoglobin (g/dL): 13.4
- Platelet Count (K/MM3): 223.5

Median of 487 days between scans

Scan 2

- Sodium (Na) (mEq/L): 138
- Creatinine: 0.8
- Albumin (g/dL): 3.8
- Alkaline Phosphatase (IU/L): 242
- AST (IU/L): 60
- Total Bilirubin (mg/dL): 0.9
- ALT (IU/L): 70
- White Blood Cell Count: 5.8
- Hemoglobin (g/dL): 13.4
- Platelet Count (K/MM3): 214.5

Outcomes

Event rate of 36.7% for main events of interest:

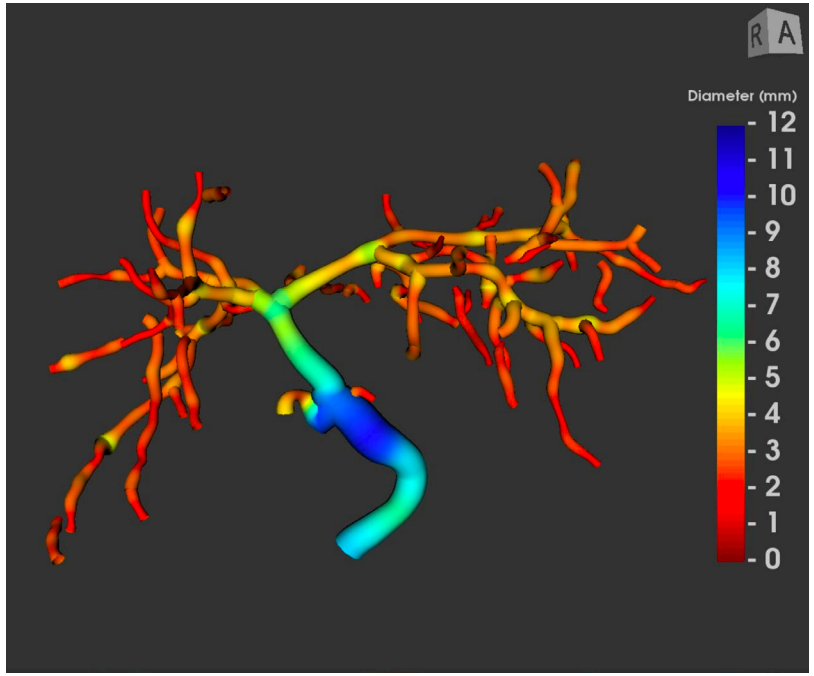
- Decompensation (N=18)
- Liver Transplant (N=12)
- Cholangitis (N=13)
- Death (N=6)

CHAMPS example MRCP+

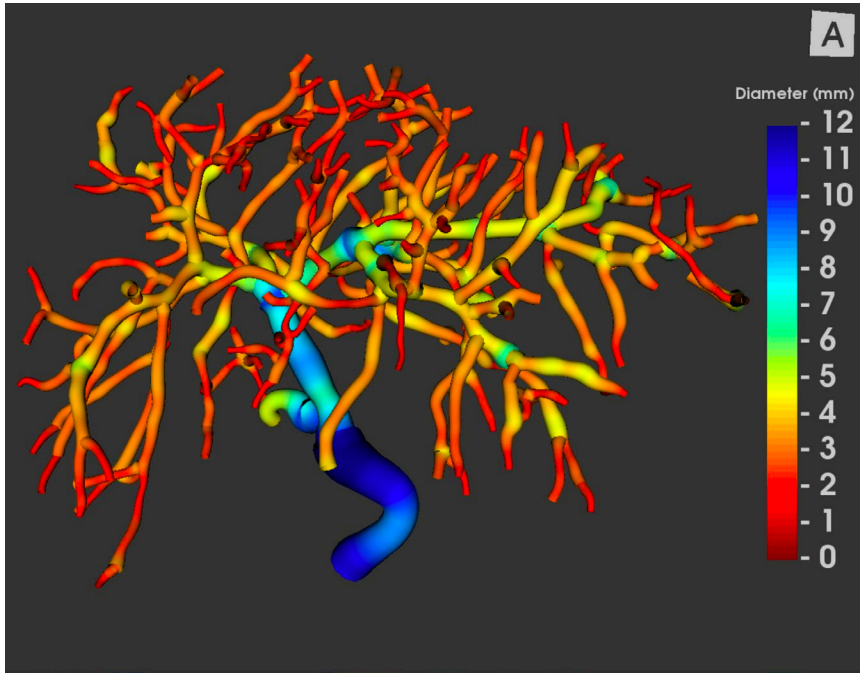
Participant information:

- Hispanic male
- Age at PSC diagnosis: 32
- Ulcerative Colitis
- Age at Scan 1: 32
- Time between scans: ~ 1 year
- 1 ERCP
- Liver stiffness (MRE): 2.8 kPa
- Bloods (Scan 1 - Scan 2):
  - ALT: 20 - 105
  - ALP: 302 - 1108
  - PLT: 391 - 432
  - Alb: 3.1 - 2.8

No event after Scan 1



Metric	
Biliary tree volume (ml)	12.8
Number of ducts	70
Number of strictures	12
Number of dilatations	24



Metric	
Biliary tree volume (ml)	37.2
Number of ducts	172
Number of strictures	27
Number of dilatations	47