AASLD Nov. 12-15, 2021

The Liver Meeting®

DIGITAL **EXPERIENCE**

The Best of The Liver Meeting®

PEDIATRIC LIVER DISEASES

About the program:

Best of The Liver Meeting 2021 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

Use of these slides:

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Patient-derived cholangiocyte organoids identify reactive ciliopathy in pathogenesis of epithelial injury in biliary atresia

Aim

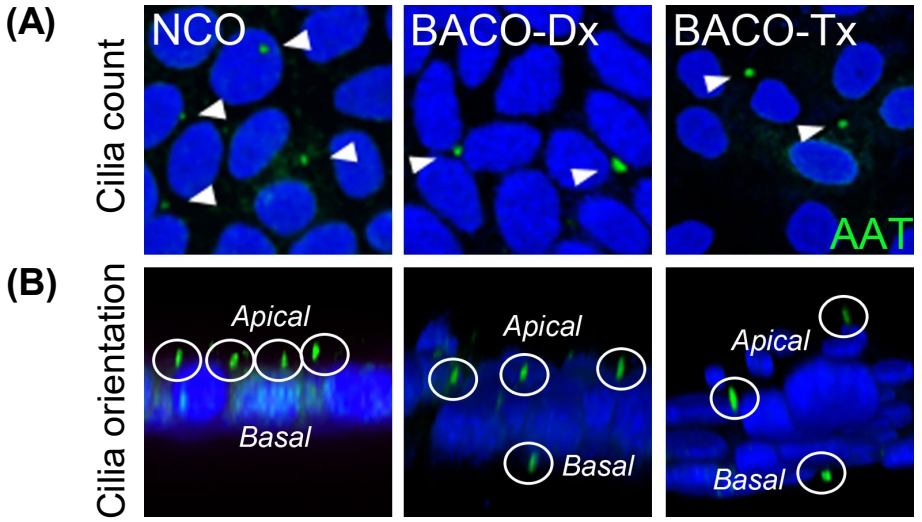
- To investigate the mechanisms of ciliary loss using patient-derived cholangiocyte organoids in biliary atresia (BA)

Methods

- Human cholangiocyte organoids derived from livers of normal donors (NCO) and BA patients at diagnosis (BACO-Dx) and transplant (BACO-Tx) were subjected to immunostaining, confocal microscopy, RNAseq analysis, and rhesus rotavirus (RRV)-infection induced injury model.

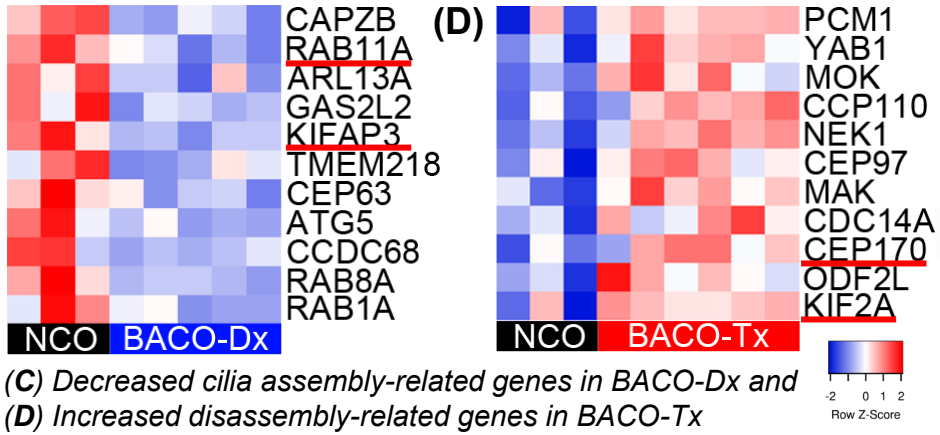
Conclusions

- Cilium is decreased and malpositioned in cholangiocytes from BA patients.
- Differential expression of genes regulating assembly & disassembly in BA organoids and normal cholangiocytes following virus infection point to cilium loss as pathogenic mechanisms of epithelial injury.

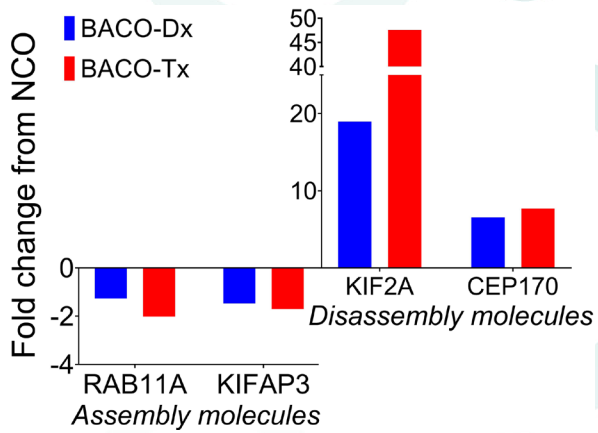


*BACOs show (**A**) decreased and (**B**) malpositioned cilia*

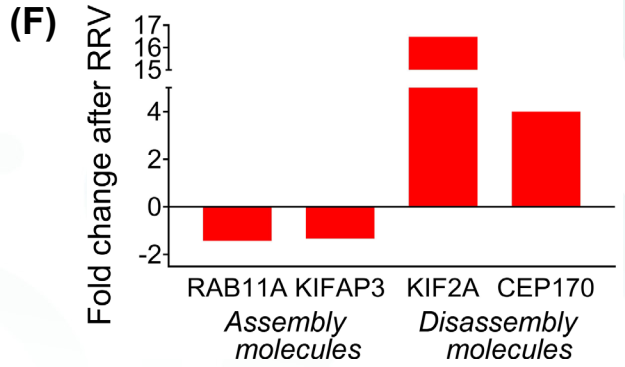
AAT: acetylated α tubulin



*(**C**) Decreased cilia assembly-related genes in BACO-Dx and (**D**) Increased disassembly-related genes in BACO-Tx*



*(**E**) Molecules regulating cilia assembly are decreased at diagnosis, and disassembly increased at transplant*



*(**F**) Expression of assembly molecules decreased and disassembly increased in NCOs after RRV infection*

Kim S, et al., Abstract 6.

TLM dX®

Accuracy of serum MMP-7 as a biomarker of biliary atresia in a large U.S. cohort

Aims

- Determine the accuracy of matrix metalloproteinase-7 (MMP-7) as a biomarker of biliary atresia (BA)
- Identify the optimal cut-off point of MMP-7 to diagnose BA
- Compare MMP-7's diagnostic performance to other clinical markers

Methods

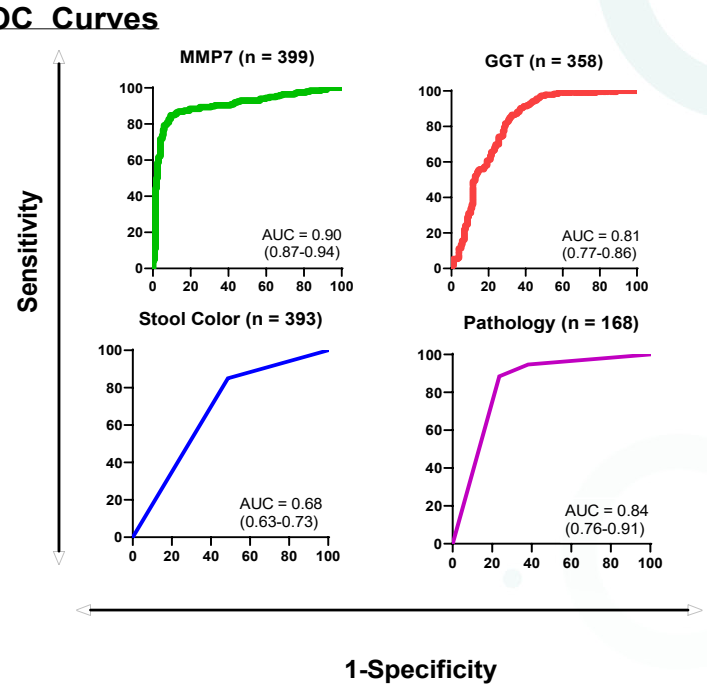
- Case control study of 399 cholestatic infants (BA=201, Non-BA=198) enrolled in the PROBE study of the Childhood Liver Disease Research Network.
- Serum MMP-7 quantified by antibody-based single-plex assay.
- Performance of MMP-7 and other biomarkers assessed by multivariate logistic regression with ROC-AUC and DeLong's test.

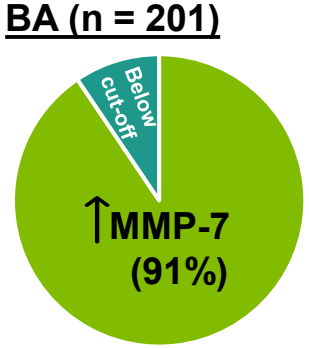
Main Findings

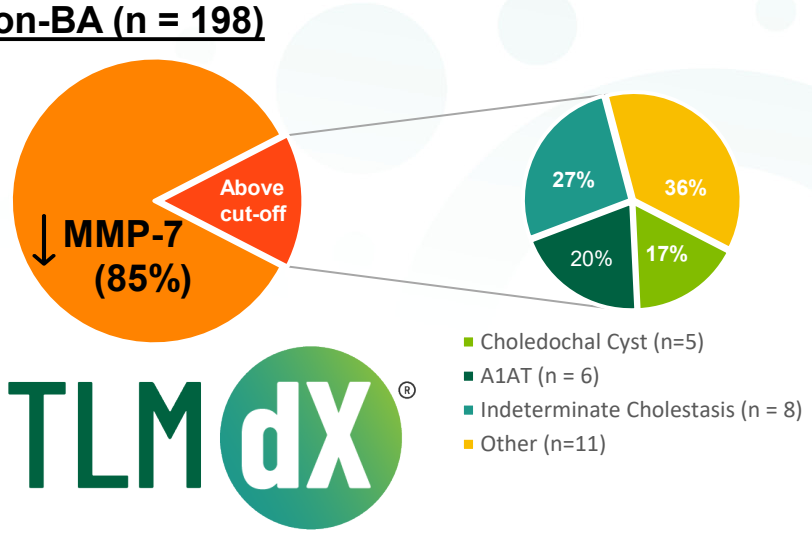
- ROC-AUC of MMP-7=0.90 (CI 0.87-0.94) was superior to GGT (AUC=0.81), acholic stool (AUC=0.68), and obstructive features in liver histology (AUC=0.84).
- MMP-7 cut-off of **67.4 ng/mL** produced sensitivity 90.5%, specificity 84.4%, positive predictive value 71.3%, and negative predictive value 95.4% for the diagnosis of BA.
- Composite AUC was not superior to AUC for MMP-7 alone.

Conclusions

- MMP-7 had a superior discriminatory value compared to other clinical markers studied.
- Low MMP-7 identifies patients unlikely to have BA (NPV 95.4%).







TLMdX®

Pandurangi, S., et al, Abstract 199.

Application of real-world evidence analytics: a 6-year event-free survival analysis in Alagille syndrome of the GALA clinical research database and maralixibat treated patients

Objective

- To compare time to first clinical event in maralixibat (MRX)-treated Alagille syndrome (ALGS) patients to the natural history Global Alagille Alliance Study (GALA) external controls

Methods

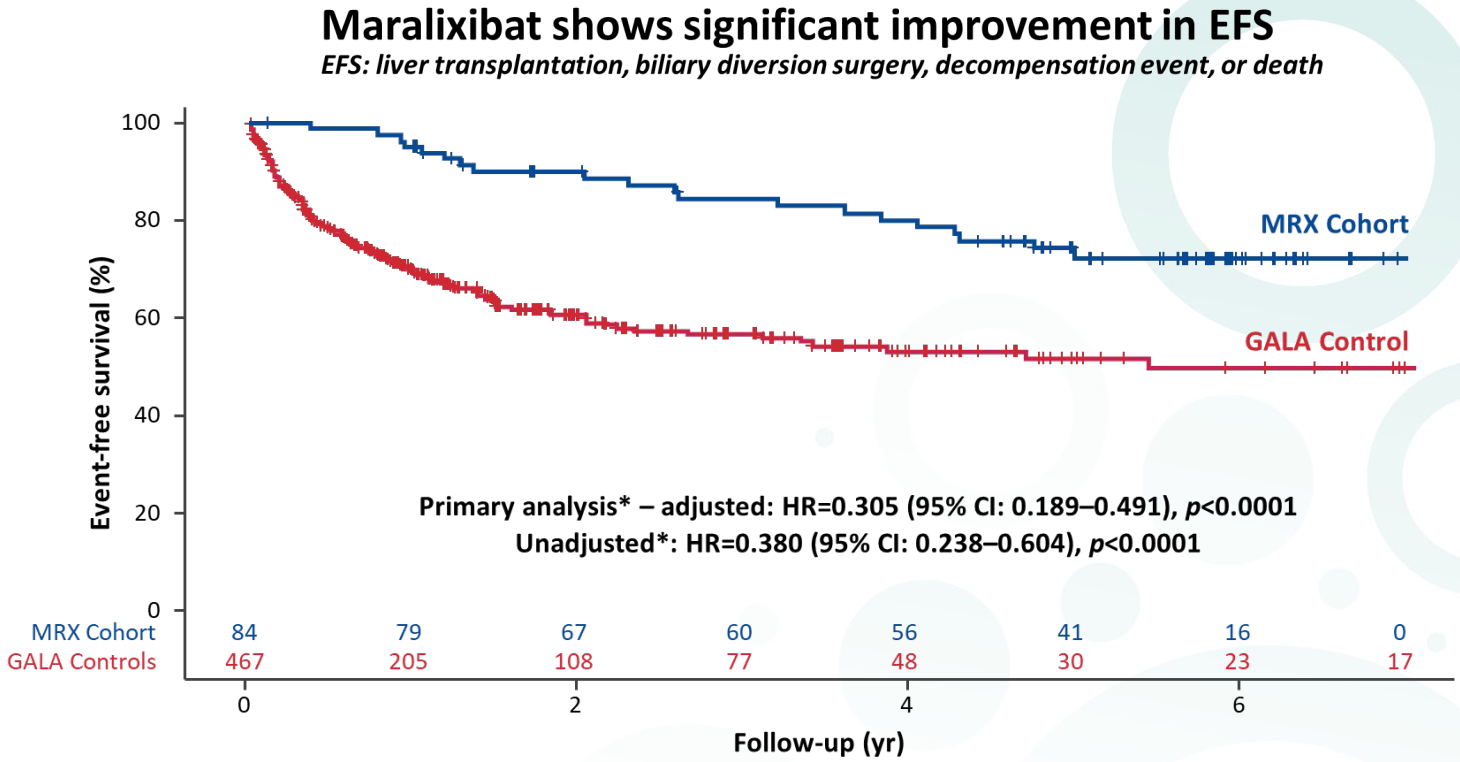
- External controls were selected from GALA and balanced in a pre-specified manner to align key MRX eligibility criteria; event-free survival (EFS) was compared, including extensive sensitivity and subgroup analyses, to evaluate robustness of findings.

Main Findings

- Patients with ALGS treated with MRX demonstrated significant improvement in 6-year EFS (p<0.0001) with consistent results observed across several sensitivity and subgroup analyses.

Conclusions

- Using this real-world evidence analytical method, a 70% reduction in clinical outcomes was observed in MRX-treated ALGS patients compared with controls from the GALA database.



CI, confidence interval; EFS, event-free survival; HR, hazard ratio; MRX, maralixibat; SAP, statistical analysis plan. * Cox regression models: Primary: Cox regression - effect of MRX vs. GALA log likelihood test adjusted for age, sex, bilirubin, and ALT (according to the SAP).

Hansen BE, et al., Abstract LO7.

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Pediatric Liver Diseases

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