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For Collaborative Research℠
Berkeley's Hub for Regulatory Science

Pediatric MASH Working Group

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Background

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- First meeting (Sept 2024)
  - Review literature, NITs, outcomes
- Subsequent meetings (N=6)
  - Focus on fit-for-purpose and feasible clinical trial design
    - Inclusion criteria, assessment of efficacy
- Status
  - Draft to be reviewed by regulators (FDA, EMA)
  - Final review and submission before EASL 2026

Inclusion Criteria

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- Hepatic steatosis with evidence of inflammation and fibrosis
  - Liver histology is an accepted method of MASH diagnosis in children
  - Non-invasive assessment of steatosis and inflammation
- Adult MASLD histology scores (MAS) should not be used in children
  - Histologic findings of **steatosis, inflammation (zones 1 and 3) and fibrosis**
  - Ballooning is not useful as an inclusion criterion or when assessing for treatment response in children

Lessons from Past Clinical Trials

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- Biopsy (if used for study inclusion) may be historical
  - Up to two years
  - Participants should have evidence of ongoing disease, as documented by continued elevation of ALT and MRI PDFF

Population of Interest in Pediatric Trials

- Children with **any fibrosis** should be included in MASLD/MASH trials
  - Study population should not be limited to those with F2 or F3

Role of NITs in Children

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- **MRI-PDFF, ALT, and GTT** were agreed upon as the best supported NIT endpoints for clinical trial for youth-onset MASH with fibrosis

- Non-invasive tests (NITs) that assess fibrosis may be used when sufficiently supported by evidence

Other Design Considerations

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- Recent Pediatric MASH guidelines on lifestyle modification (i.e., sugar reduction, increased physical exercise, and encouragement to see a dietician) should be implemented in future youth-onset MASH trials as standard of care treatment.

Areas for Future Research

- Additional outcomes (secondary or exploratory) should measure safety (e.g., height, creatinine, pubertal stage), liver improvement (e.g., CT1, MR-elastography, NIS2+, ELF), metabolic response (e.g., BMI, lipids, blood pressure), and explore use of novel biomarkers.

Next Steps

- Distribute for input from regulators
- Prepare manuscript for publication