

Berkeley

 School of
Public Health

 **EASL**
European Association
for the Study of the Liver



**Forum for
Collaborative HIV Research**

A large, light grey circular graphic in the background, featuring a white geometric pattern of overlapping squares and lines, with a small orange square at the center, similar to the Forum for Collaborative HIV Research logo.

Status of Pediatric NASH Research

Liver Forum 5
November 10, 2016

Cysteamine Bitartrate Delayed-
Release for the Treatment of
Nonalcoholic Fatty Liver
Disease in **C**hildren

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DECISIONS

Drug
Choice

Dose
Choice

Who
to Treat

End Point



NASH CRN CyNCh

End Point

1st trial in pediatric liver disease designed with liver histology as the primary outcome

PRIMARY OUTCOME

End Point

The proportion of children with histologic improvement in NAFLD between the baseline liver biopsy and follow-up biopsy after 52 weeks of treatment, where improvement was defined as:

1. decrease in NAS of 2 points or more and
2. no worsening of fibrosis.

Who
to Treat

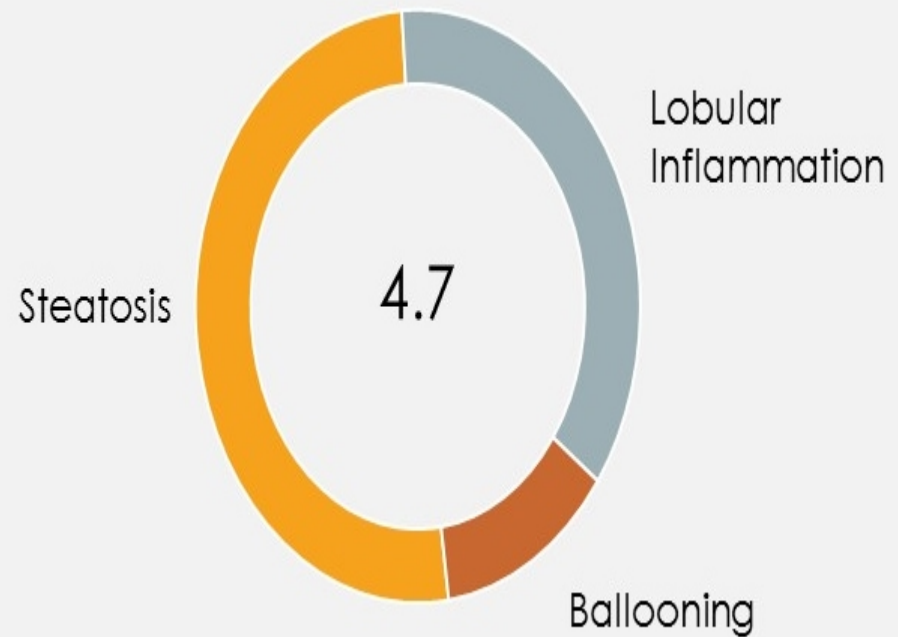
HISTOLOGIC ENTRY CRITERIA

- $NAS \geq 4$

Who
to Treat

HISTOLOGIC ENTRY CRITERIA

- $NAS \geq 4$



Dose
Choice

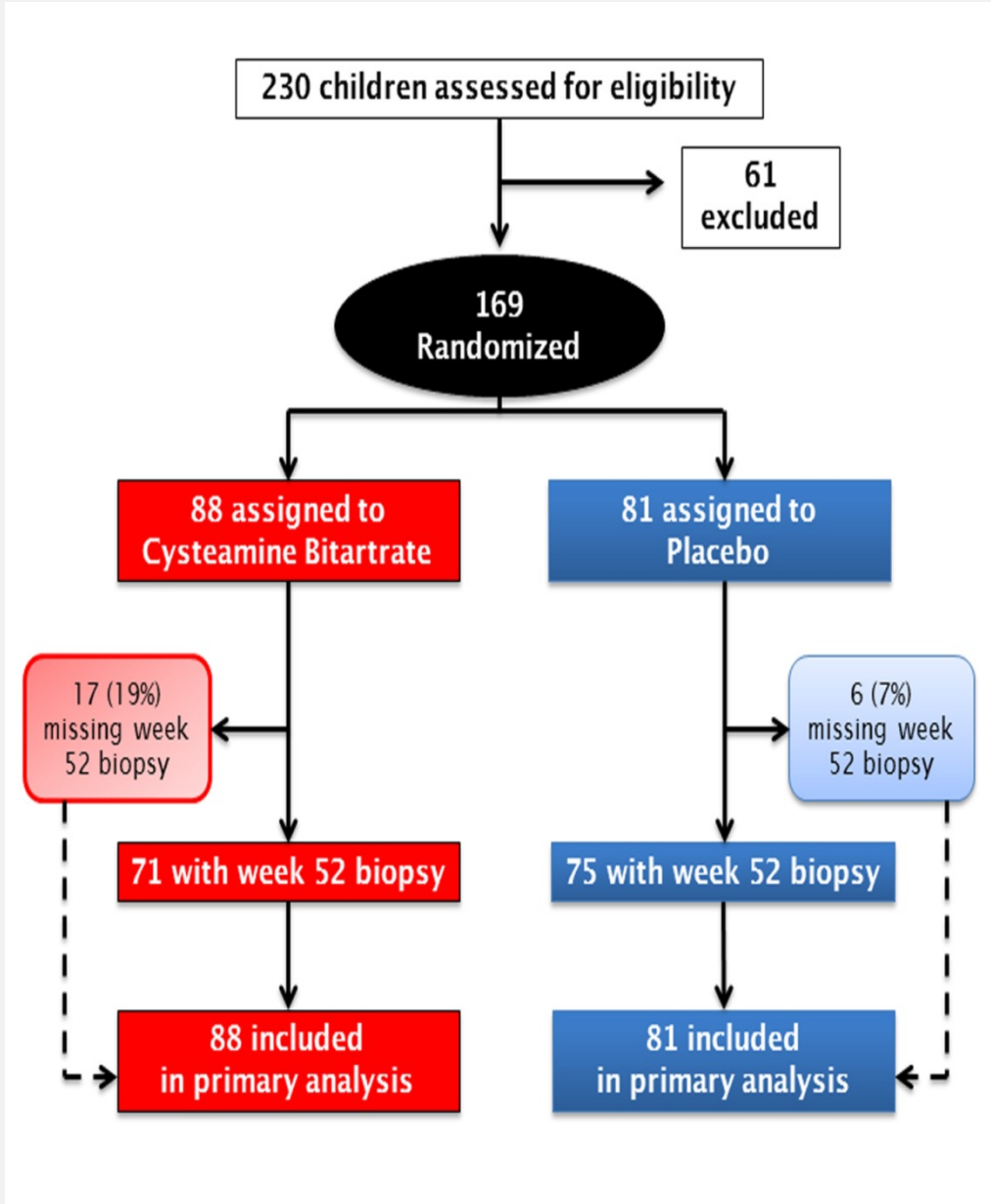
WEIGHT BASED DOSING STRATA

Weight	Dose
≤ 65 kg	300 mg BID
>65 to 80 kg	375 mg BID
> 80 kg	450 mg BID

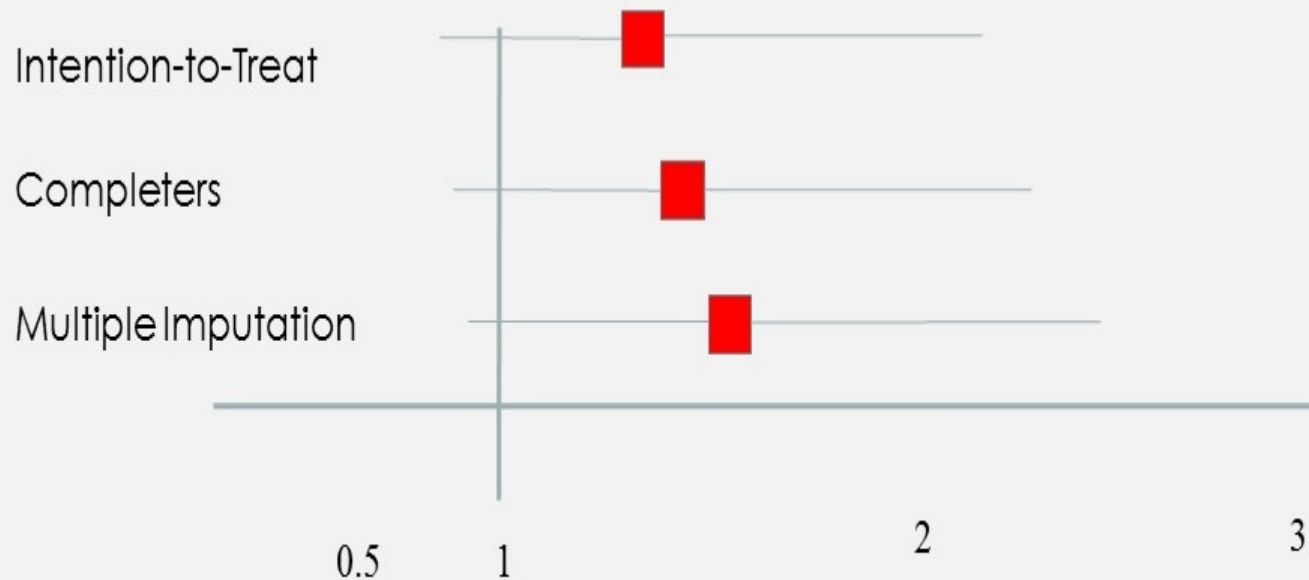
Drug Choice

Who to Treat

End Point



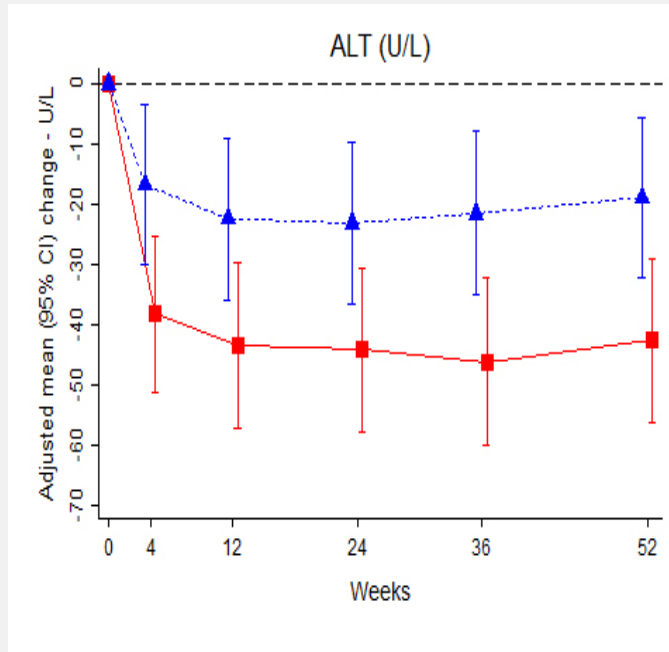
CYSTEAMINE BITARTRATE DID NOT IMPROVE NAFLD ACTIVITY SCORE



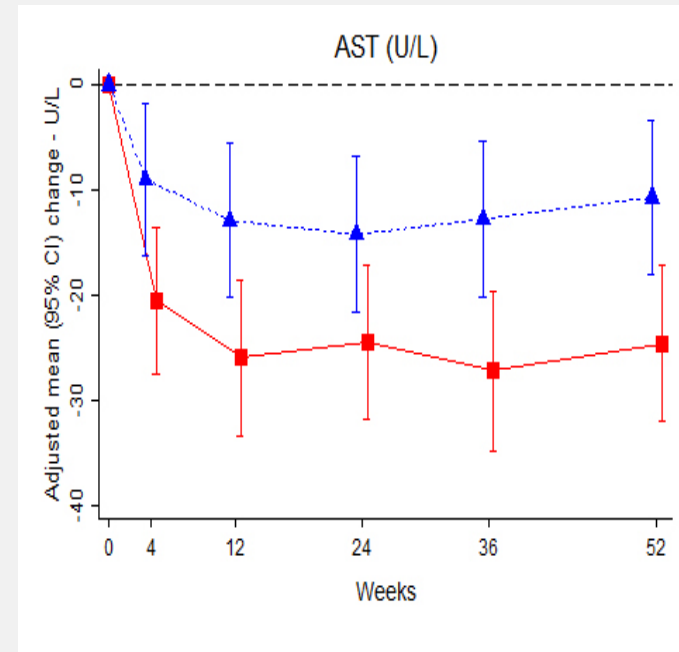
CYSTEAMINE BITARTRATE IMPROVED ALT AND AST

▲ Placebo

■ Cysteamine Bitartrate



P < 0.01

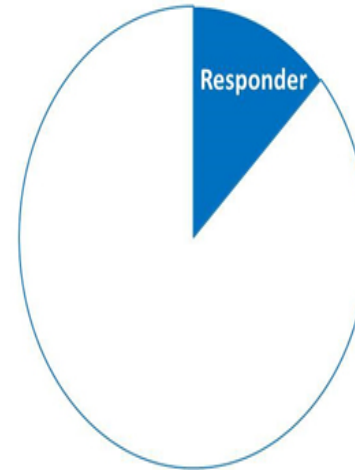
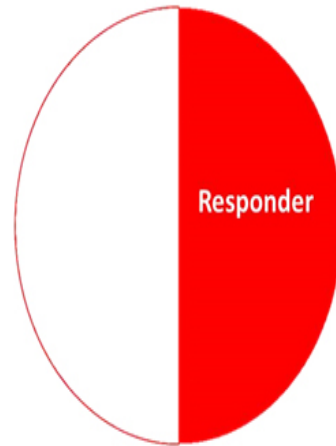


P < 0.001

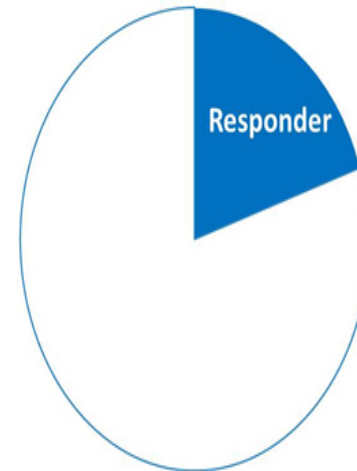
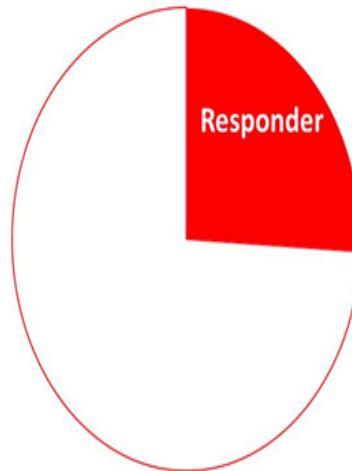
Cysteamine Bitartrate

Placebo

≤ 65 kg

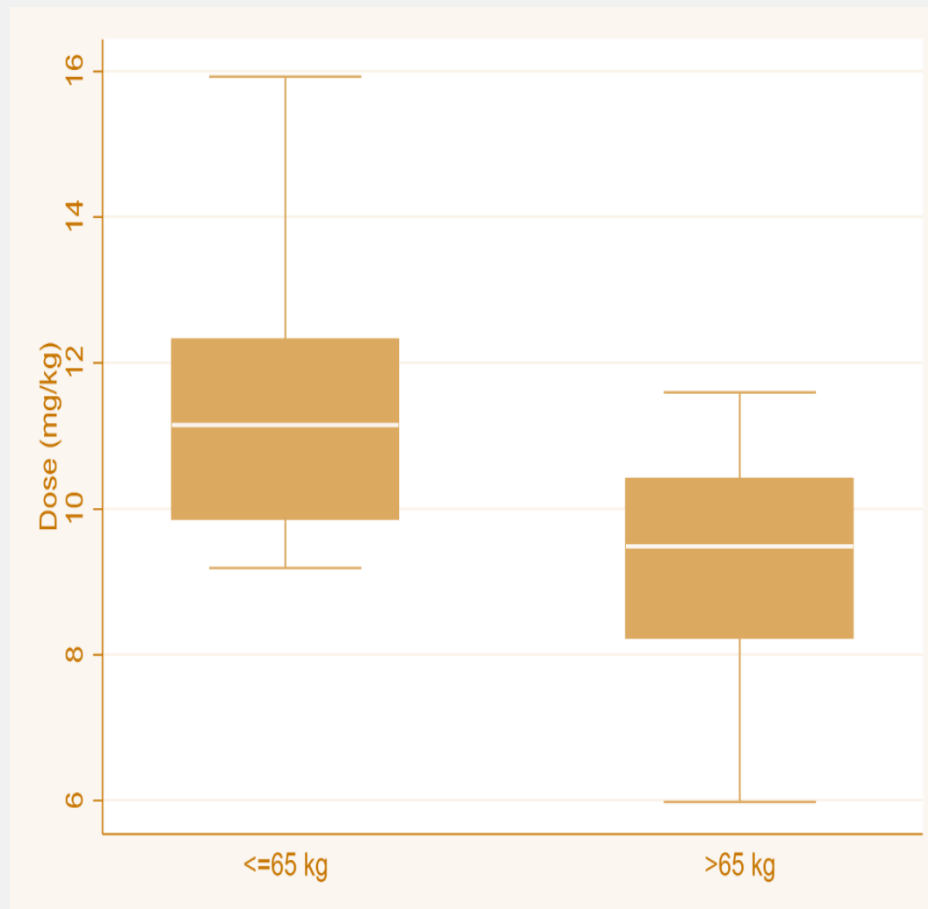


> 65 kg



P < 0.01

CHILDREN < 65 KG RECEIVED
SIGNIFICANTLY HIGHER DOSE (MG/KG)



P < 0.0001

HISTOLOGIC IMPROVEMENT BY DOSE (MG/KG) TERTILES



WEIGHT BASED DOSING STRATA

Weight	Dose	Capsules per day
≤ 65 kg	300 mg BID	8
>65 to 80 kg	375 mg BID	10
> 80 kg	450 mg BID	12

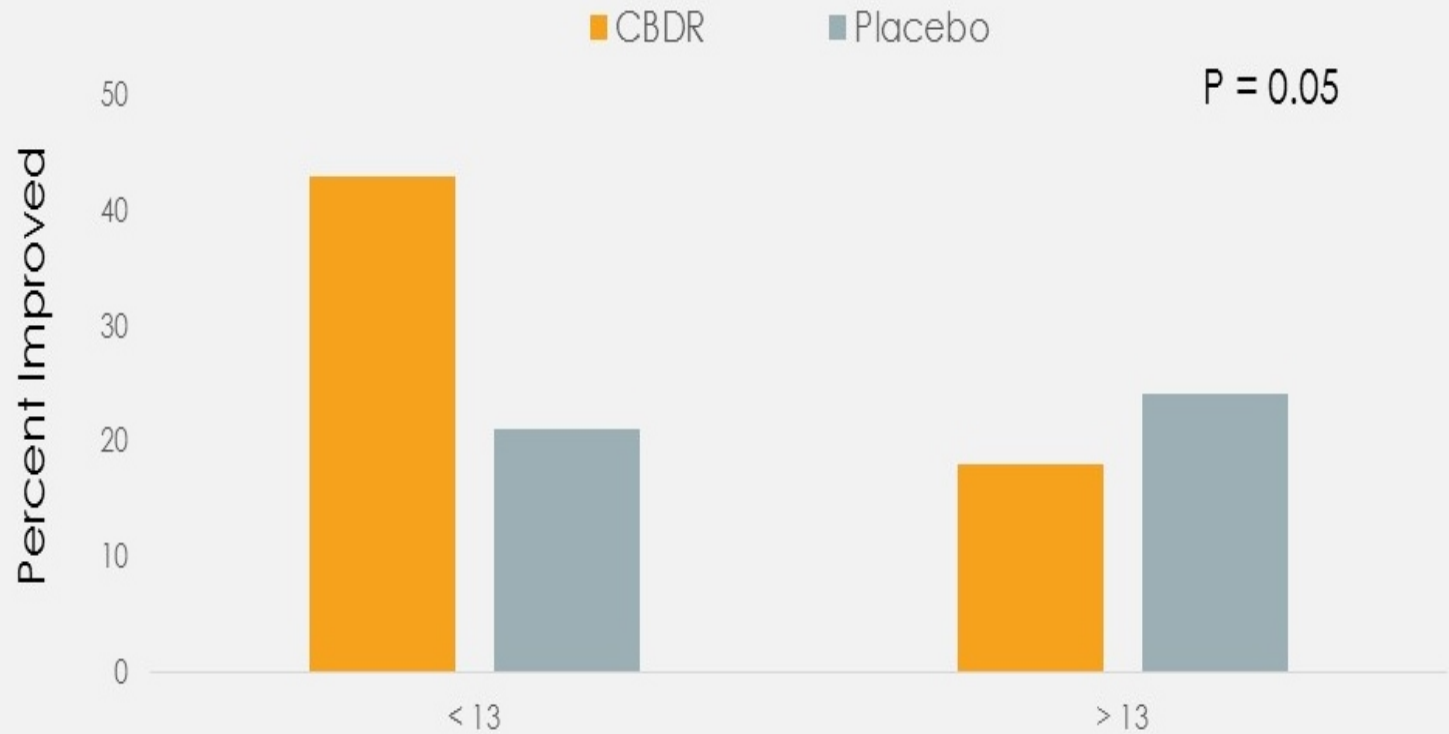




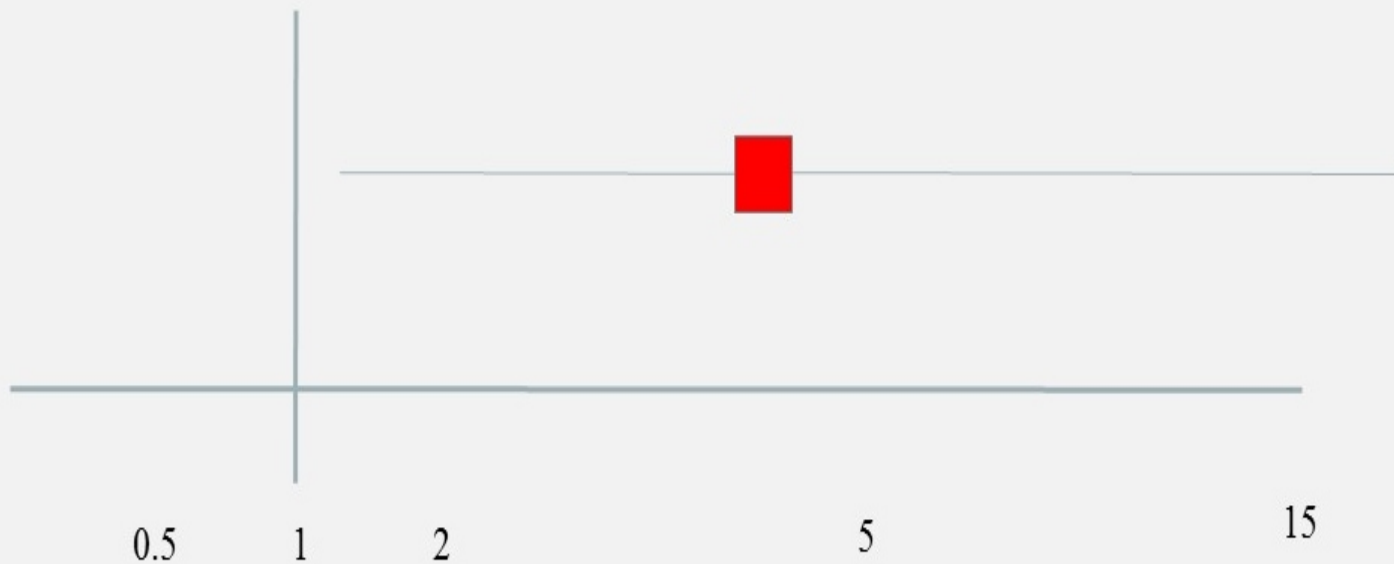
WEIGHT GAIN

- Lifestyle counseling c/w AAP Guidelines
- Mean weight gain = 7.1 kg
- 1.3 pounds per month

HISTOLOGIC IMPROVEMENT BY AGE



IMPROVEMENT IN TYPE 2 OR BORDERLINE PORTAL NASH WITH CYSTEAMINE BITARTRATE



QUESTIONS

Drug
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