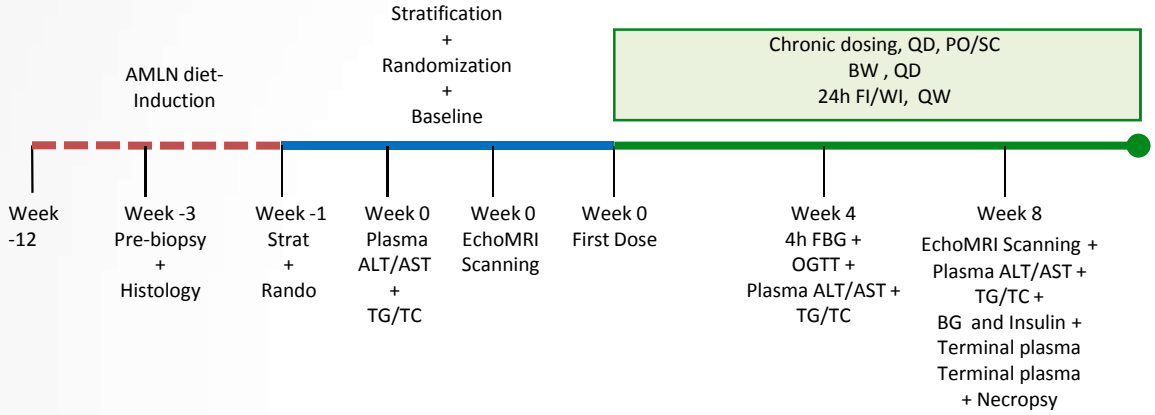
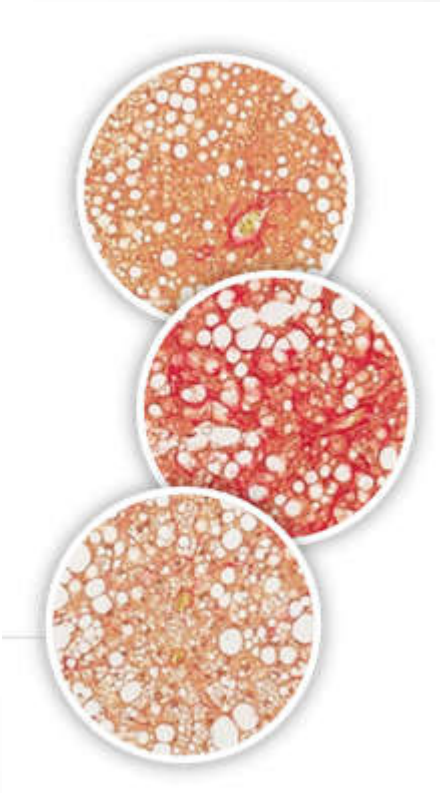
Male ob/ob NASH mice

Standard Study outline



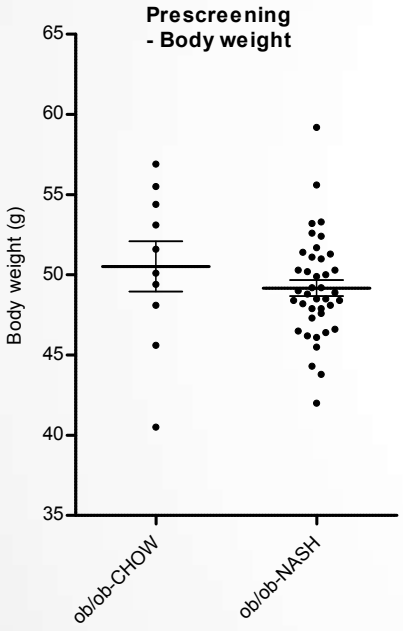


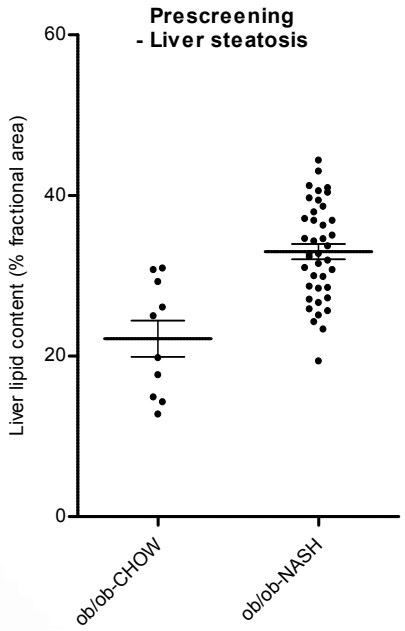
DIO NASH golden standard study:

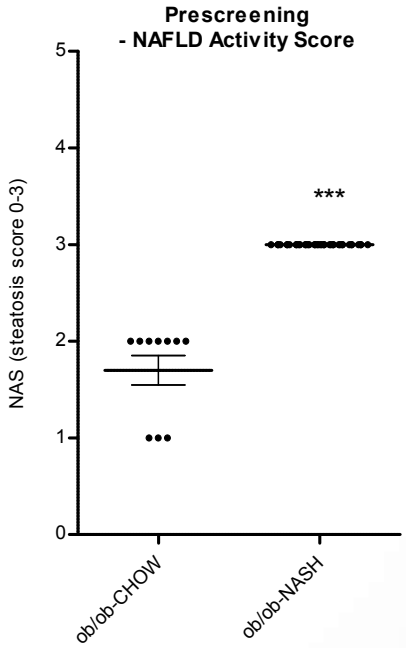
- 80 ob/ob NASH mice fed AMLN diet (40% HFD, 18% fructose, 2% cholesterol) for 12-14 weeks.
- Ob/ob-NASH mice pre-screened and randomized into 5-6 groups of n=12 based on liver biopsy and histological assessment (scoring) of fibrosis (Sirius Red) and steatosis (H&E) progression.
- Total of 8 weeks of QD/BID dosing SC/PO.
- Pre-study EchoMRI and EchoMRI scanning at study end.
- Plasma ALT, AST, TG and TG at baseline, week 4 and at termination.
- Blood glucose (4h fasting) at week 4 followed by OGTT (week 4).
- Blood glucose and plasma insulin (4h fasting) at study end.
- Terminal liver removal and analyses of fibrosis (Sirius Red, hydroxyproline), steatosis (H&E), liver TG and TC (extraction).
- Terminal NAFLD Activity Score and Fibrosis Stage (delta values compared to pre-study biopsies).
- Terminal liver RNA extraction for optional RNAsequencing

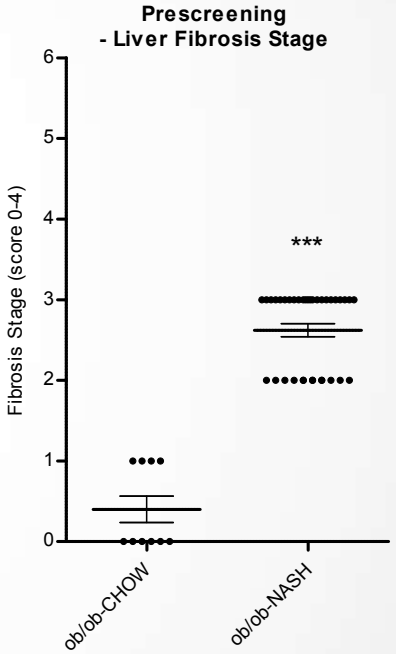
Baseline prescreening

Body weight and prebiopsy histology and pathology

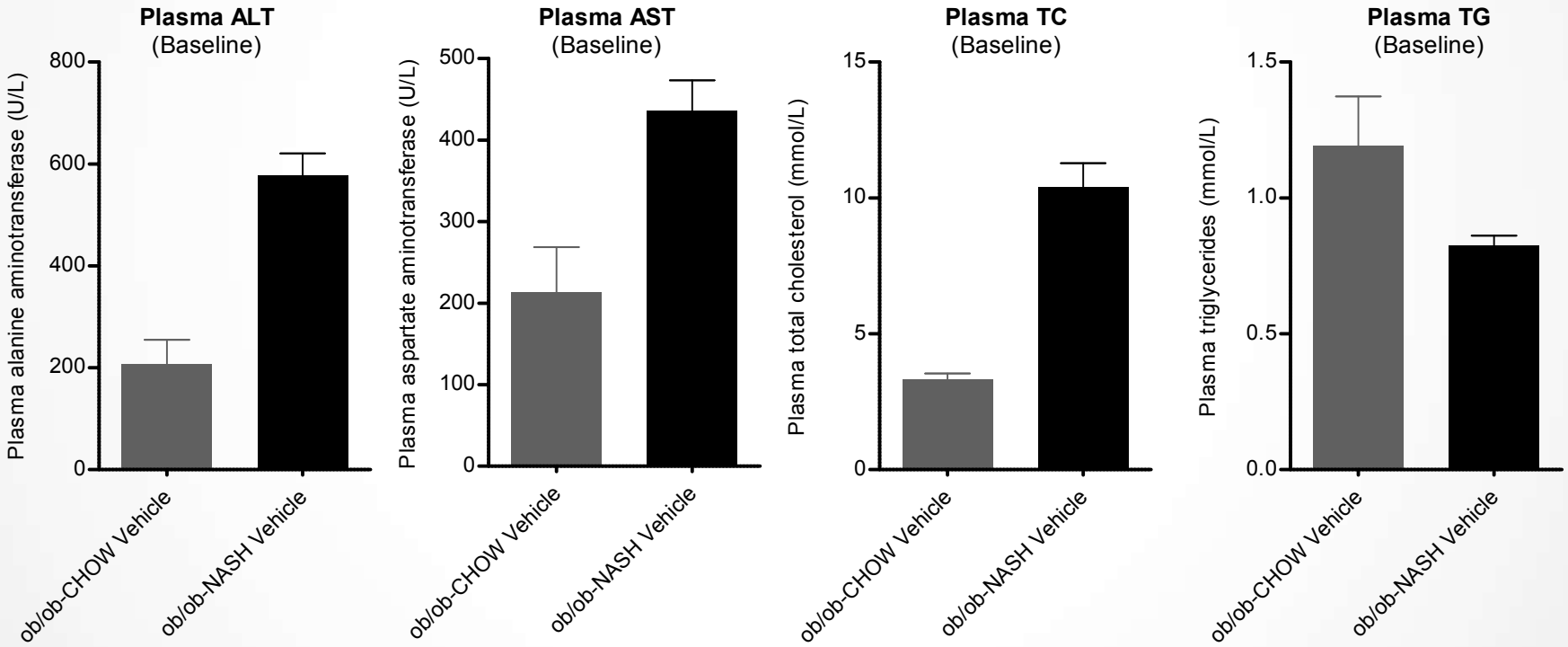






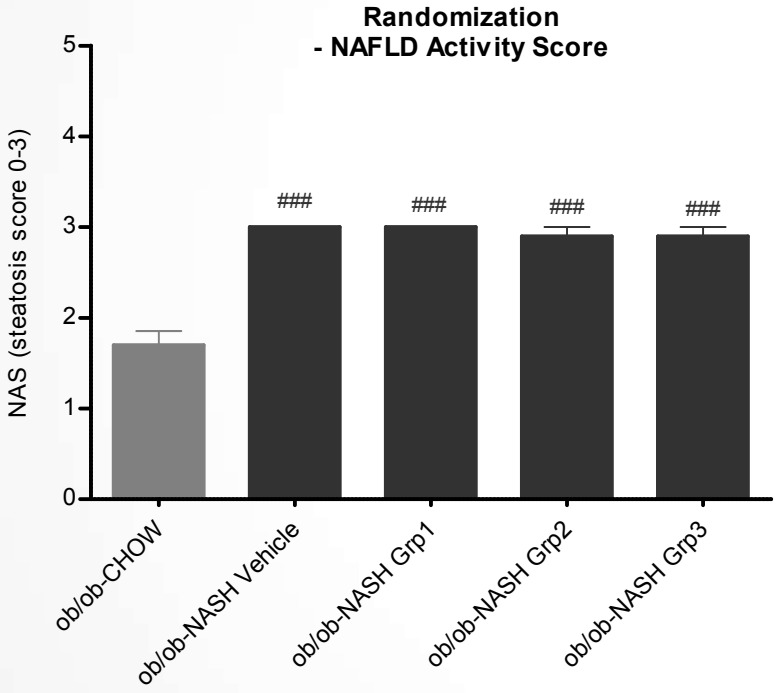


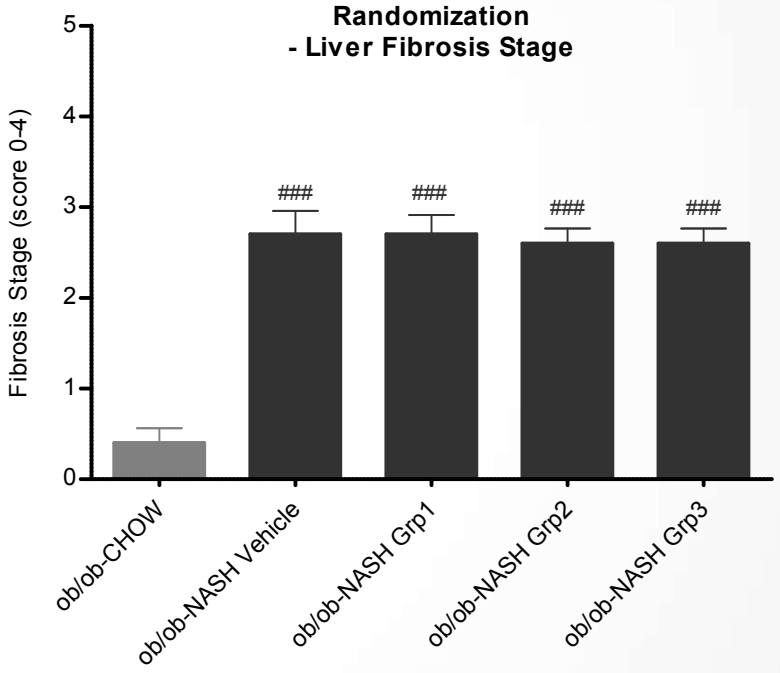
Baseline – Liver plasma enzymes



Baseline NASH characteristics

Randomization based on prebiopsy





Baseline DIO characteristics