Metabolic, biochemical, histopathological, and transcriptomic effects of resmetirom (MGL-3196) in the GAN diet-induced obese and biopsy-confirmed mouse model of NASH

Authors: Michael Feigh1, Jacob Nørh-Meldgaard1, Sanne S. Veidal1, Martin Rann Madsen1, Henrik H. Hansen1
1Gubra, Hørsholm Kongevej 118, Hørsholm, Denmark

Corresponding author: Michael Feigh - mfe@gubra.dk

Background & Aim

Resmetirom (MGL-3196), a selective THR-β agonist, has been recently been reported to improve liver histological outcomes in a clinical trial for non-alcoholic steatohepatitis (NASH). The present study aimed to evaluate the metabolic, biochemical, histopathological and transcriptomic effects of resmetirom treatment in the Guba-Amylin NASH (GAN) diet-induced obese (DIO) mouse model of fibrosing NASH.

Study outline

Improvement in NAFLD Activity Score

Improvement in quantitative histology of steatosis and stellate cell activation

Hepatic transcriptomic profile for fibrosis and inflammation

CONCLUSION

- Resmetirom (MGL-3196) reduces hepatomegaly, plasma ALT and liver total cholesterol.
- Resmetirom promotes 22-point significant improvement in NAFLD Activity Score.
- Fibrosis stage was unaffected by Resmetirom.
- Resmetirom reduces quantitative histological markers of steatosis and stellate cell activation.
- Resmetirom demonstrated minor effects on fibrosis-associated gene expression.
- These findings agree with clinical findings, further highlighting clinical translatability of the GAN DIO-NASH mouse model.