

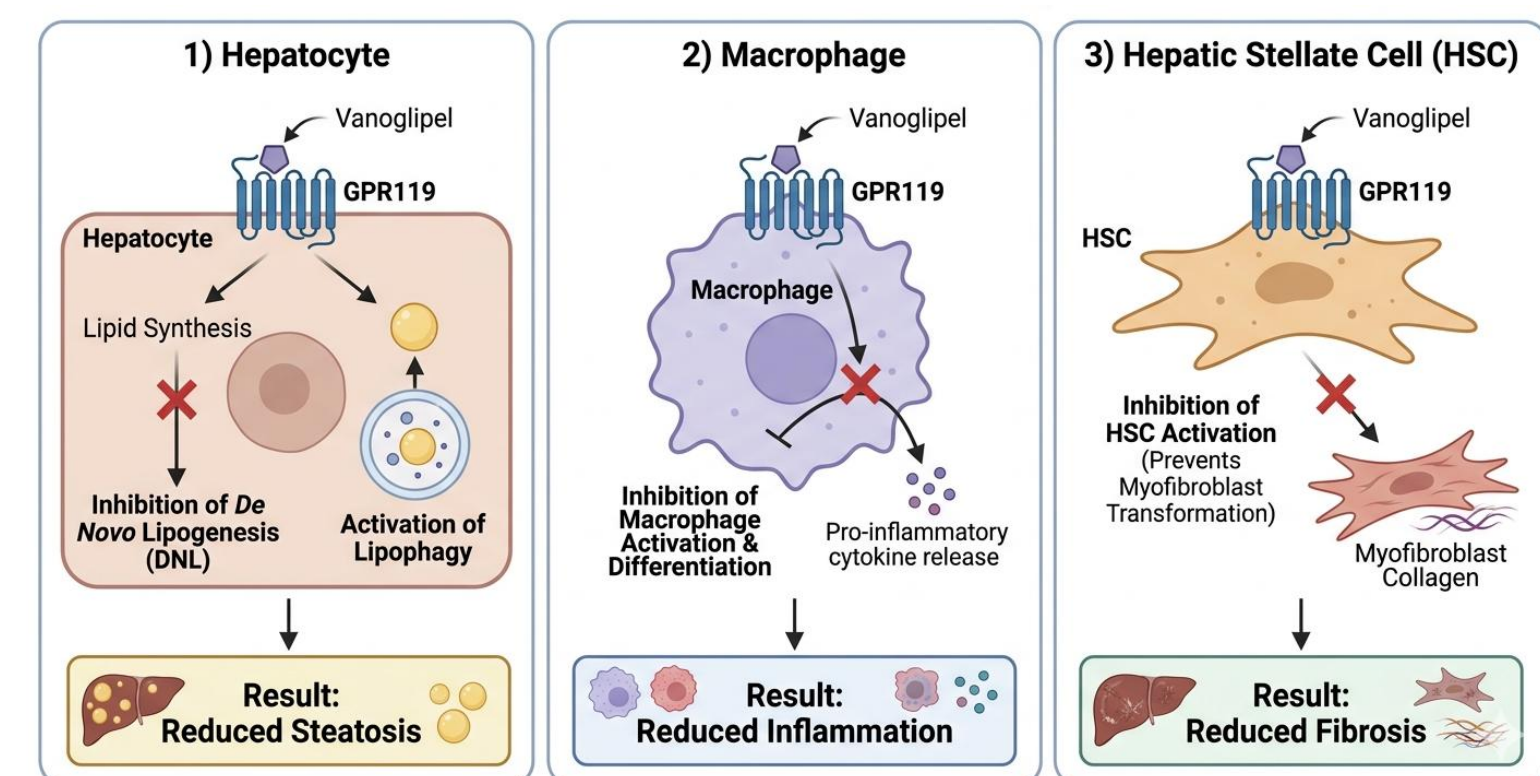
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Please refer to Poster 2856-LB for additional data on Vanoglipel

BACKGROUND

- Vanoglipel (DA-1241), a first-in-class potential GPR119 agonist, successfully demonstrated hepatoprotective effects along with improved glucose and lipid control in presumed MASH patients in the US (Phase 2a, NCT06054815)



OBJECTIVE

- To evaluate the efficacy of vanoglipel plus resmetirom in DIO-MASH mice
- To assess whether combination therapy confers enhanced metabolic benefits beyond either agent alone

METHODS

Animal Model & Study Design

Male C57BL/6J mice were fed the Gubra-Amylin NASH diet (40 kcal-% fat, 22% fructose, 10% sucrose, 2% cholesterol) for 39 weeks to induce biopsy-confirmed MASH. Mice meeting inclusion criteria (NAS ≥5; steatosis 3; inflammation ≥2; fibrosis F2-F3) were stratified by PSR fractional area and fibrosis stage, randomized into 4 groups (n = 16-18), and treated for 16 weeks. Statistical analysis: Treatment effects were analyzed using multiple-comparison tests with correction for multiplicity.

Treatment Groups

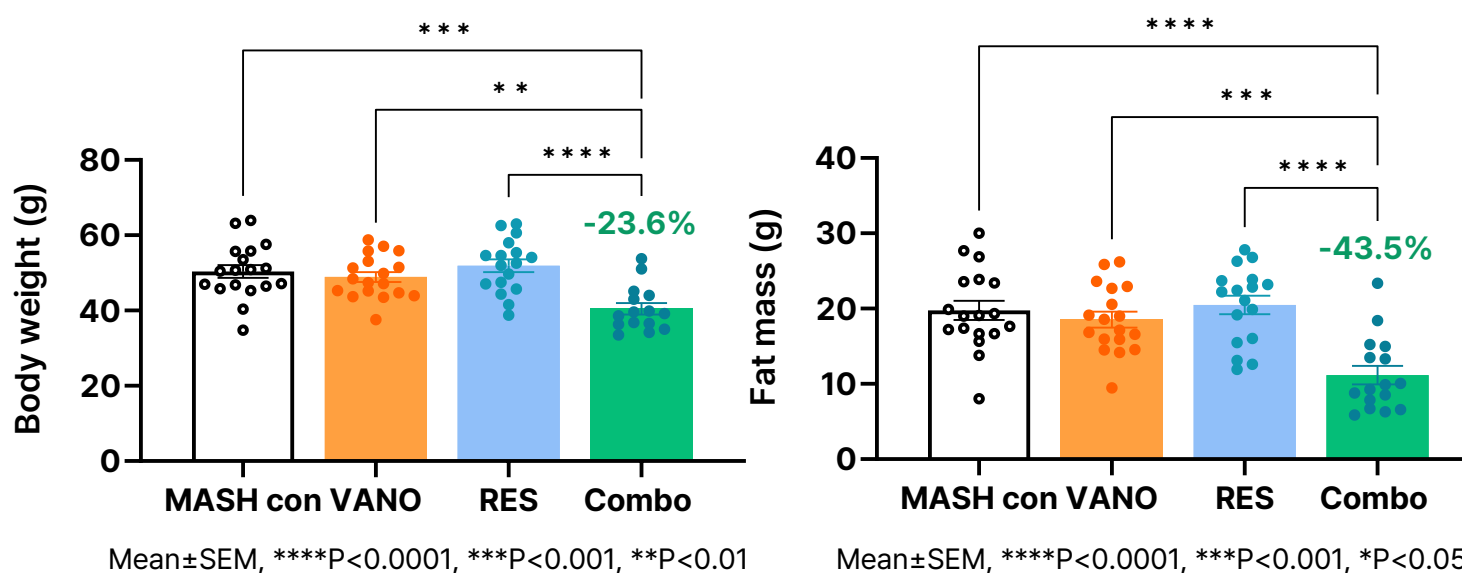
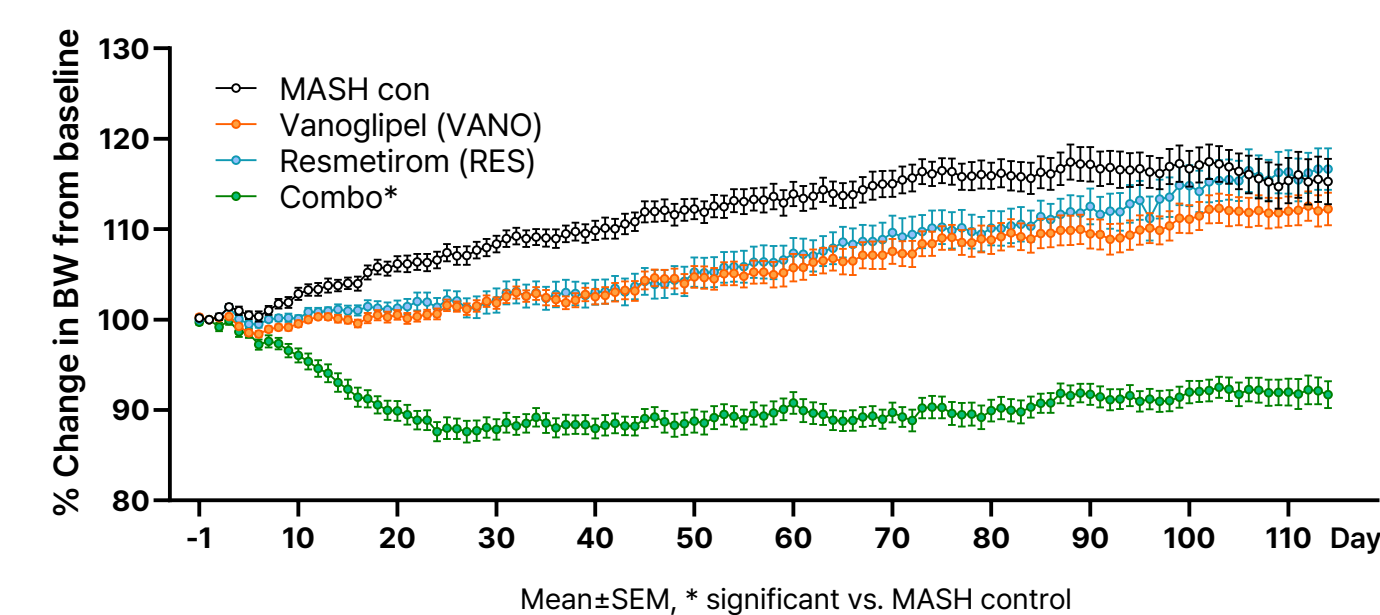
GROUP	TREATMENT	DOSE (MG/KG/DAY)
Control	GAN diet + vehicle	NA
Vanoglipel	Vanoglipel (DA-1241), in diet	100
Resmetirom	Resmetirom, in diet	3
Combo	Vanoglipel + Resmetirom, in diet	100 + 3

Drugs were formulated into the GAN diet at fixed concentrations (vanoglipel 0.133%, resmetirom 0.004%, w/w) and administered ad libitum; doses (mg/kg/day) represent target daily intake based on mean food consumption.

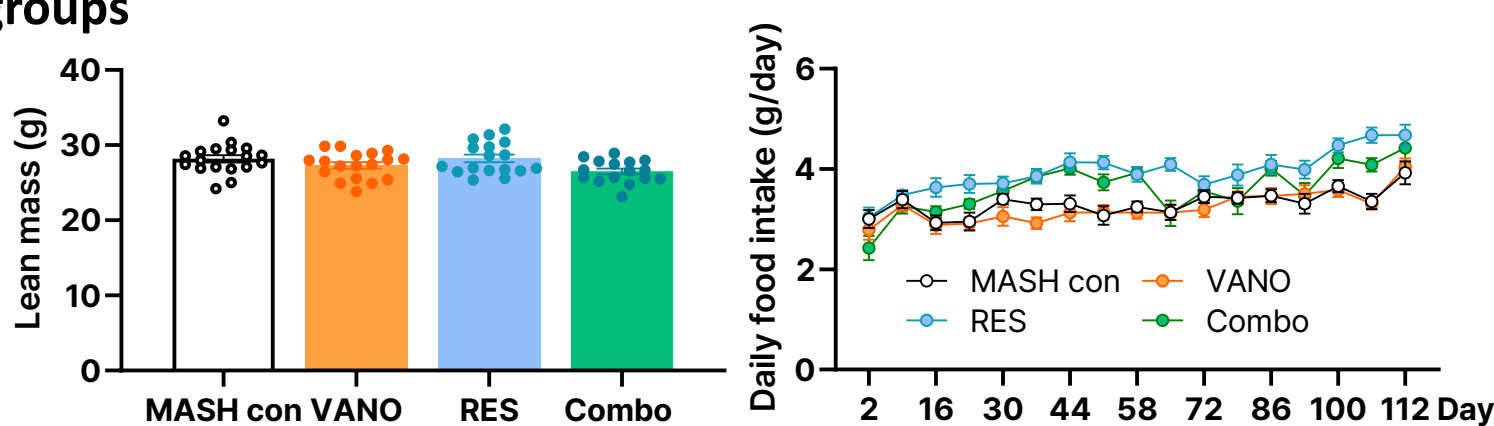
RESULTS

1 The combined use of Vanoglipel and Resmetirom exhibited significant body weight reduction unlike their monotherapy

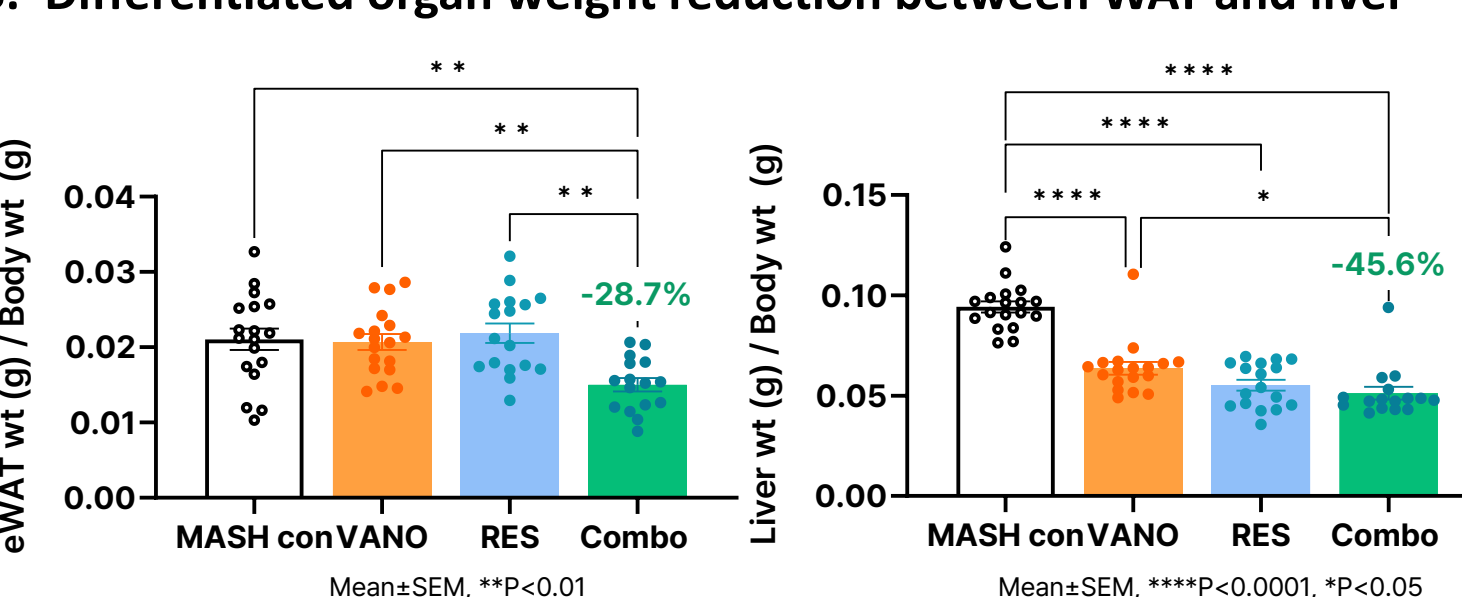
1. Significant body weight reduction only in the combination group



2. No effects on lean mass and energy intake across all treatment groups

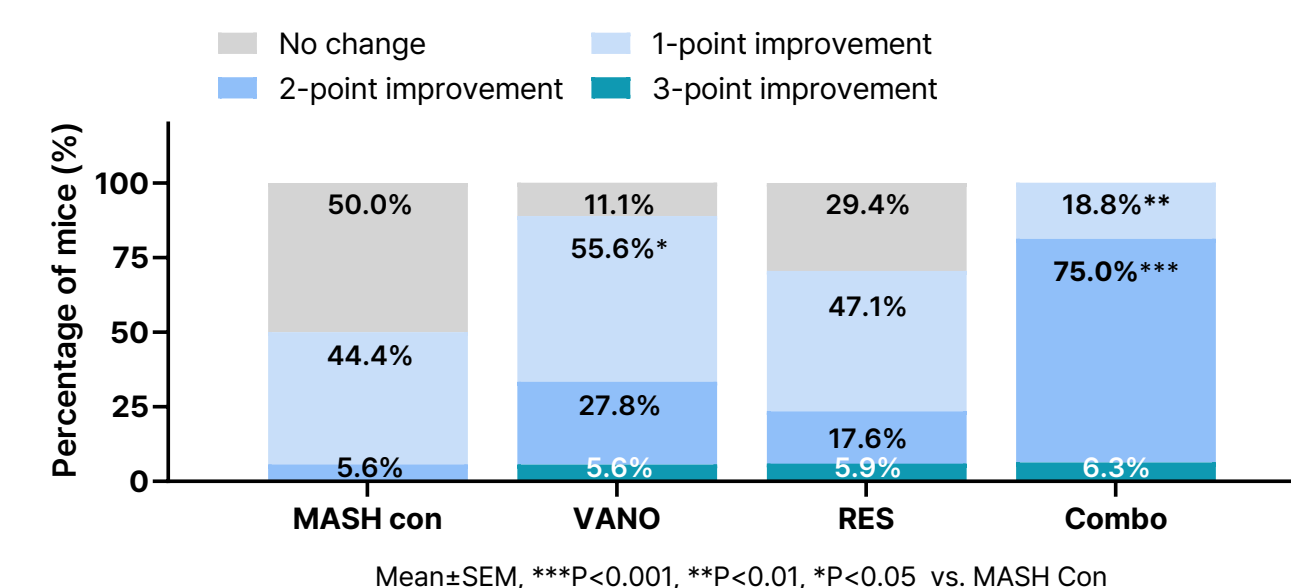


3. Differentiated organ weight reduction between WAT and liver

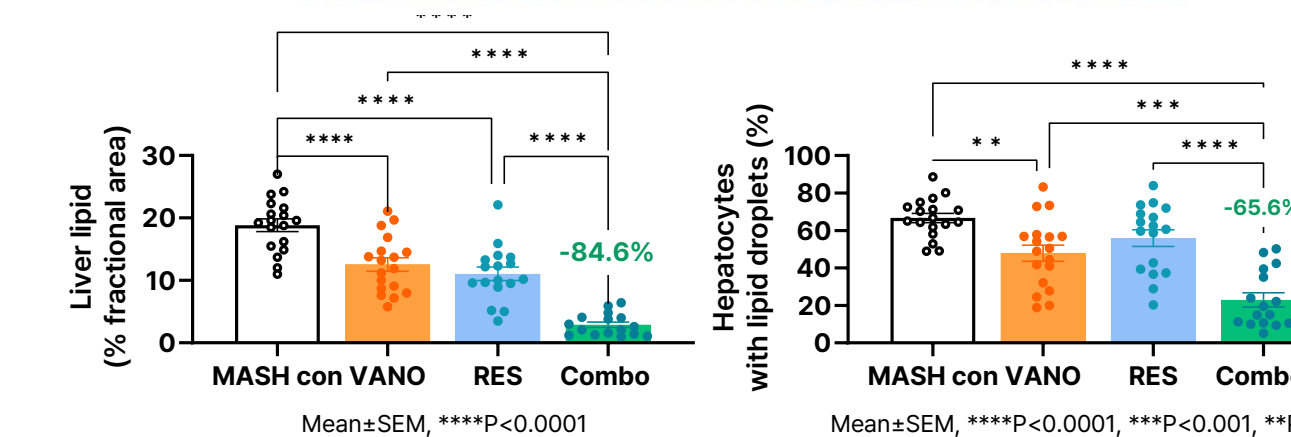
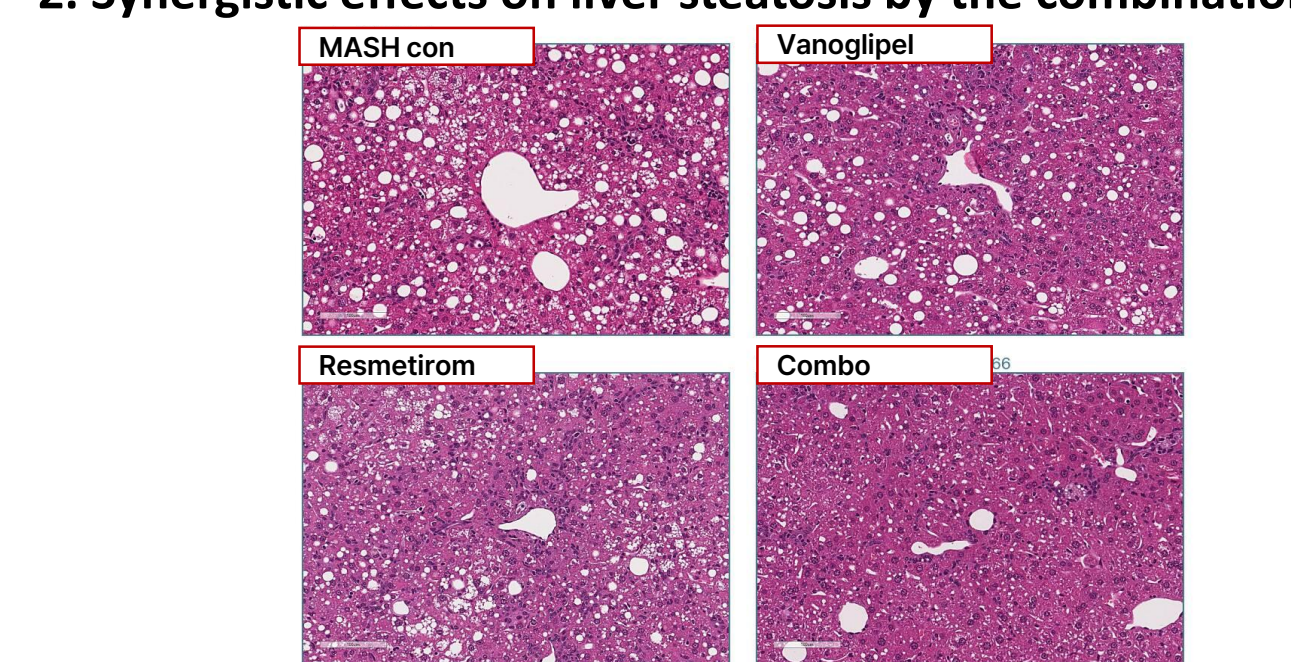


2 The combined use of Vanoglipel and Resmetirom showed synergistic improvement in liver steatosis and inflammation

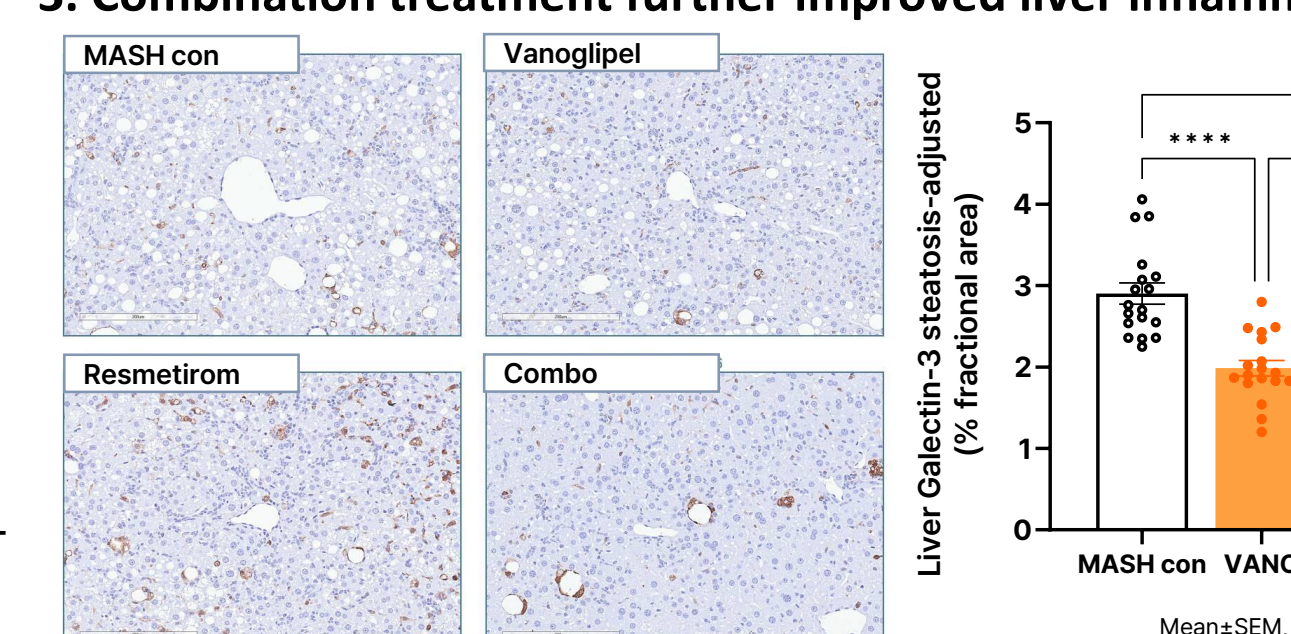
1. Synergistic NAS improvement in the combination group



2. Synergistic effects on liver steatosis by the combination

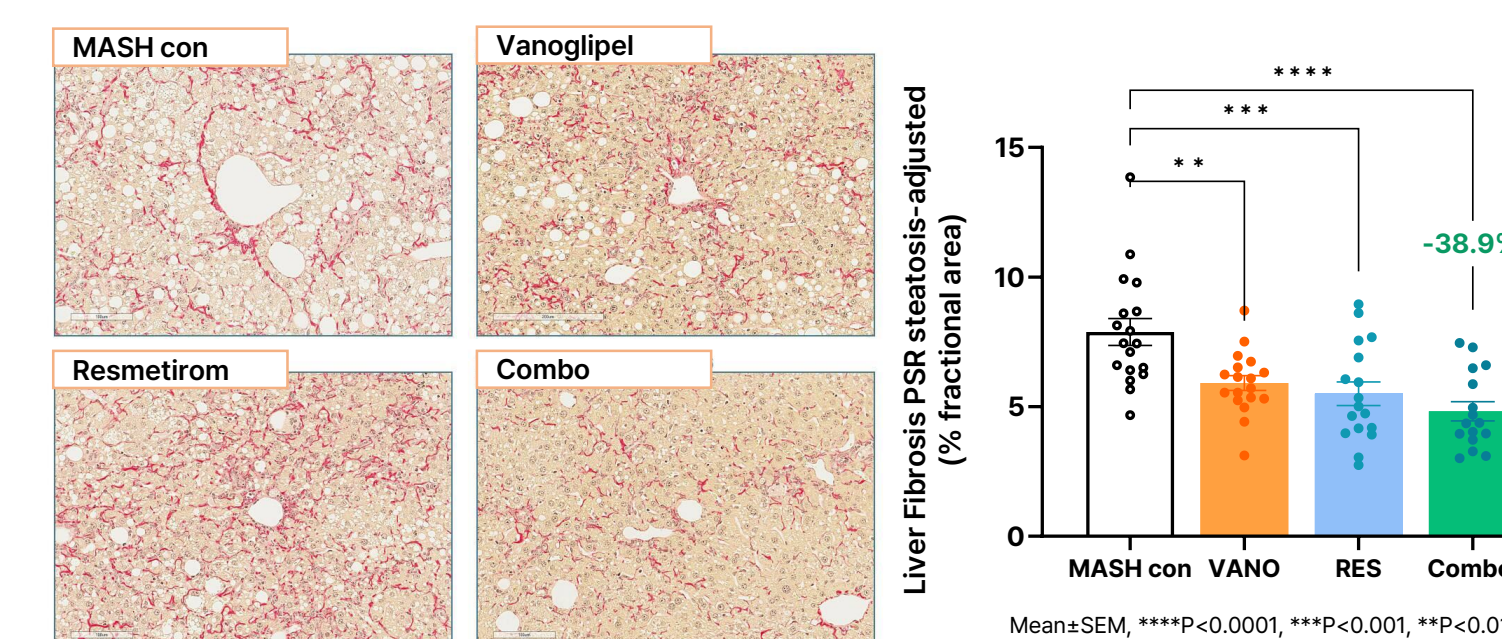


3. Combination treatment further improved liver inflammation

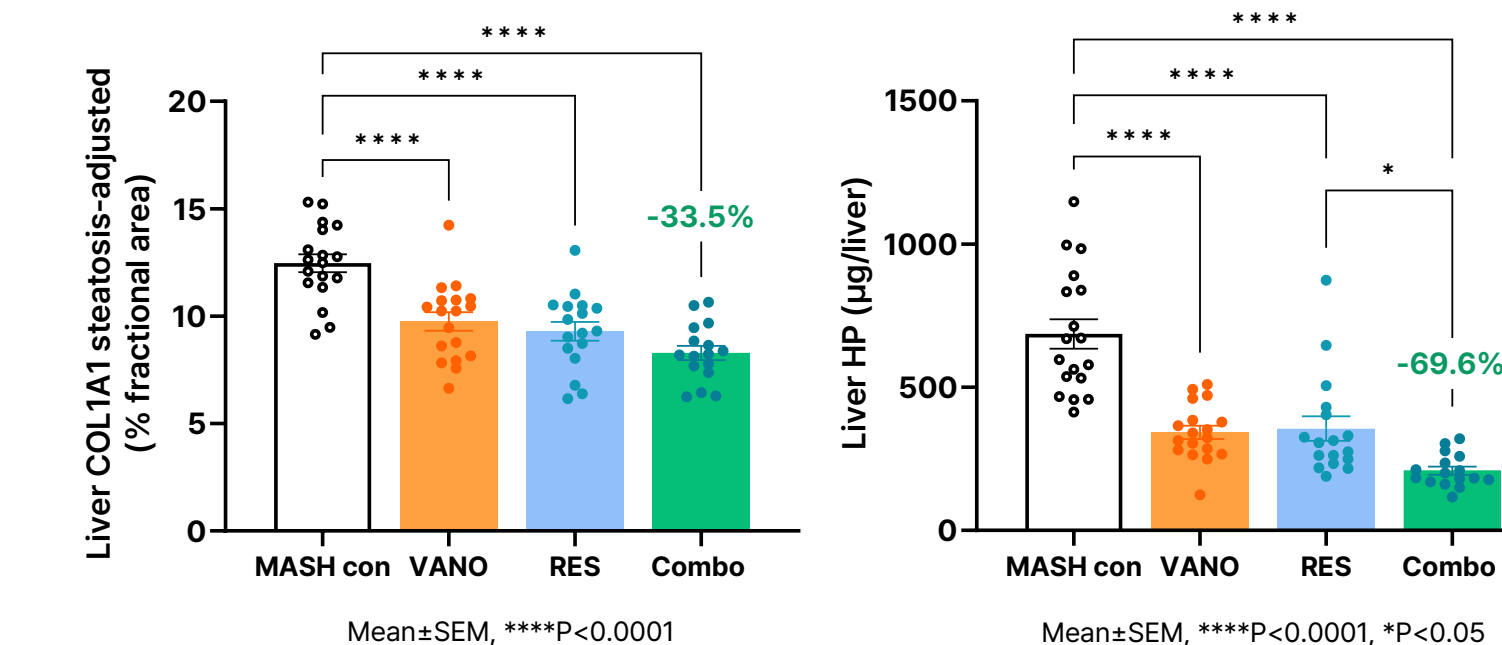


3 The combined use of Vanoglipel and Resmetirom resulted in further improvement in liver fibrosis compared with their monotherapy

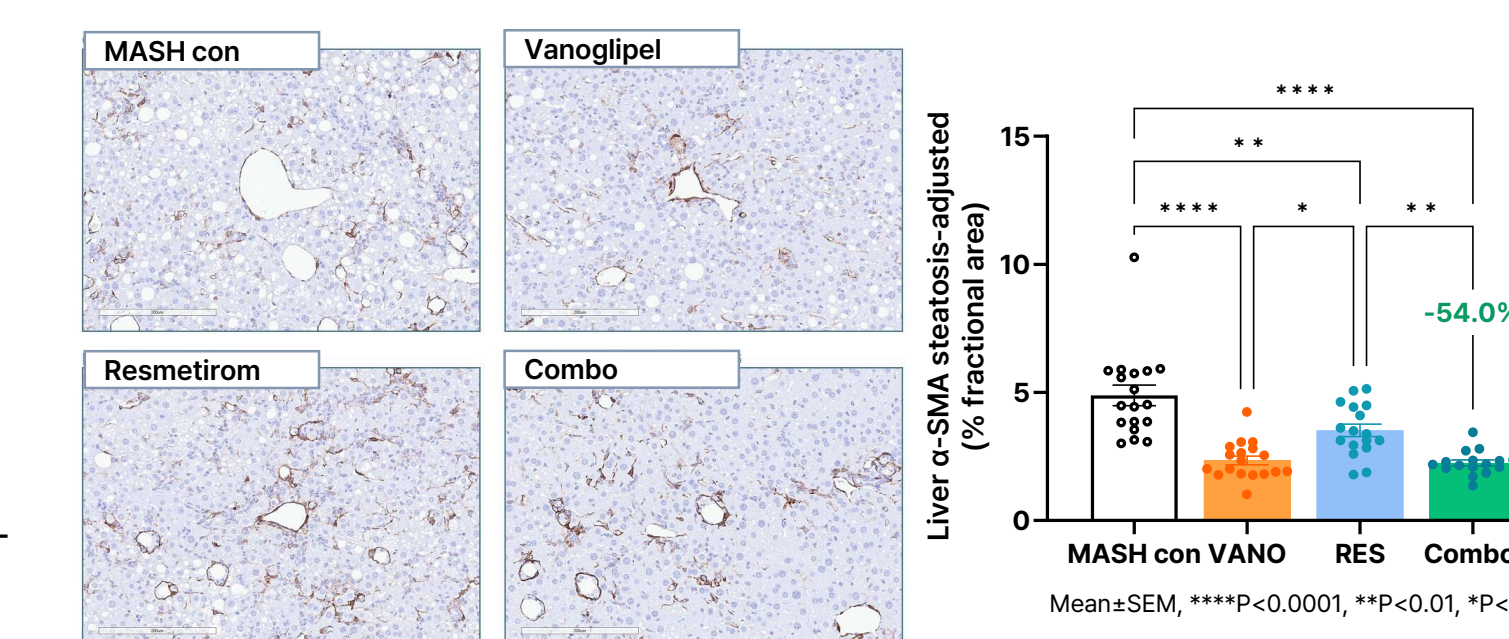
1. Significant reduction in liver fibrosis with decreased fibrosis markers



2. Additional improvement in liver injury by the combination



2. Decreased stellate cell activation across all treatment groups but most evident in the combination group



CONCLUSION

- Vanoglipel unlocks synergistic benefits when combined with resmetirom, addressing both extrahepatic drivers and intrahepatic pathology of MASH.
- The combination also achieved the greatest histopathologic improvement across markers including NAS, hepatic lipid %, α-SMA, hydroxyproline, COL1A1, and Galectin-3.
- The body weight loss observed with the combination treatment is presumed to be attributable to enhanced thermogenesis in white adipose tissue (WAT), and transcriptomic analysis is ongoing to determine the underlying mechanism.
- If translated into clinical practice, this combination therapy may provide additional metabolic benefits, including enhanced weight loss and improved glycemic control.

[Potential Hypothesis]

