GEMCABENE ATTENUATES THE NAFLD ACTIVITY AND FIBROSIS SCORES AND DOWNREGULATES HEPATIC INFLAMMATORY GENES IN THE STAMM™ MURINE MODEL OF NASH-HCC

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INTRODUCTION

Recent clinical trials have shown that improvements in NASH or fibrosis are dependent on combined hepatic lipid-lowering and anti-inflammatory strategies. Prior research on the role of gemcabene (GEM), a novel oral pan-sterol regulator, showed that such effects were translation from rodent to humans (1, 2, 3), and therefore a murine model of NASH-HCC may be adequate for a proof-of-concept experiment on the effect of gemcabene on hepatic steatosis plus fibrosis.

METHODS

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Forty-eight two-day-old neonatal C57BL/6 male mice randomized to 1 of 5 groups of 8 animals each were initially administered a single dose of vehicle (Group 1) or gemcabene (Group 2). At four weeks of age, animals were randomized to receive either gemcabene (10 mg/kg; Group 3) or vehicle (10 mg/kg; Group 4). All groups were sacrificed at 12 weeks. Histomorphology (with anti-inflammatory and anti-fibrotic effects in STAMM™ mice) is generally used as a positive comparator.

RESULTS

GEMCABENE NAS COMPOSITE SCORE

Inflammation and Fibrosis Scores Were Reduced Across All Doses of Gemcabene

Compared with the Vehicle in NASH Group

Compared with NASH in NASH Group

CONCLUSIONS

This effect of gemcabene on the liver histology and gene-expression levels associated with inflammation is complementary to our prior findings in diabetes (1). The current study provides a consistent evaluation of gemcabene as a potential new drug for treatment of NASH.

REFERENCES