INTRODUCTION

• Nonalcoholic steatohepatitis (NASH) represents an epidemic health crisis with broad impact on public health.
• Developing therapeutics for NASH poses a vexing challenge, which requires invasive procedures such as liver biopsy.
• Several inexpensive, simple, commonly used non-invasive tests (NITs), such as AST to platelet ratio index (APRI) and FIB-4 index, have been used to identify high-risk NASH patients from primary care settings.
• Ratio of triglyceride and HDL (TG/HDL) is a simple index that not only provides a rapid assessment of cardiovascular risk, but also correlates with histological improvement in NASH.
• Aldafermin (previously known as NGM282) is a non-tumorigenic FGF19 analogue that significantly inhibits bile acid synthesis, reduces steatosis, and ameliorates hepatic inflammation and fibrosis in patients with NASH.

AIM

• Using well-characterized, prospective cohorts of patients with NASH enrolled in aldafermin phase 2 trials, we aimed to investigate the effects of aldafermin on several widely-used, inexpensive NITs.

METHOD

• In part 1 of the study, 82 subjects were randomized to aldafermin 3mg (n=27) or 6mg (n=28) vs. placebo (n=27) as a daily SC injection for 12 weeks.
• In part 2 of the study, 94 subjects received open-label aldafermin 0.3mg (n=23), 1mg (n=49) or 3mg (n=22) for 12 weeks for dose-ranging finding.
• Key inclusion criteria included biopsy-proven NASH with NAS ≥4 (at least 1 point in each component), Stage 1-3 fibrosis and absolute liver fat content (LFC) by MRI-PDFF ≥8%.
• APRI, FIB-4, fatty liver index (FLI) and ratio of triglyceride and HDL (TG/HDL) were evaluated at baseline (BL) and week 12 (W12).

RESULTS

• At baseline, mean APRI, FIB-4, FLI and TG/HDL values were similar across all groups.

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<tr>
<th>Table 1 Baseline NITs Values</th>
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<tr>
<td>APRI</td>
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<td>Placebo (n=27)</td>
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<td>Aldafermin 3mg (n=27)</td>
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<td>Aldafermin 6mg (n=28)</td>
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<td>Aldafermin 1mg (n=49)</td>
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• At week 12, aldafermin-treated patients showed reductions in NITs of fibrosis (APRI and FIB-4), fatty liver (FLI) and cardiovascular risk (TG/HDL ratio); in contrast, no improvement was seen with placebo-treated subjects.
• Improvements were observed as early as 2 weeks on aldafermin and were maintained throughout treatment duration.

CONCLUSIONS

• Although liver biopsy is considered the gold standard for the diagnosis of liver fibrosis and NASH, it is impractical to use for the estimated >25 million patients with NASH in the US and Europe.
• There is an urgent need for non-invasive, easy-to-perform, cost-effective, and widely-available markers to assess disease severity and response to treatment.
• Aldafermin therapy produced improvements in several simple and inexpensive NITs of liver fibrosis (APRI, FIB-4), steatosis (FLI) and cardiovascular risk (TG/HDL ratio).
• These NITs may be useful for monitoring early treatment response to aldafermin.

ACKNOWLEDGEMENTS

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REFERENCES

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