Lipid Management in a 24-Week, Randomized, Double-Blind, Placebo-Controlled Study of Aldafermin (NGM282)

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INTRODUCTION

• Aldafermin (previously known as NGM282), an engineered FGF21 analog, significantly inhibits bile acid synthesis and regulates metabolic homeostasis.1–5

• In a 24-week, randomized, double-blind, placebo-controlled study in NASH patients with paired liver biopsies, aldamer treatment resulted in liver fat reduction, fibrosis improvement and NAS resolution.1

• However, aldamer increased serum cholesterol levels by inhibiting CYP7A1, which encodes the rate-limiting enzyme in the conversion of cholesterol to bile acids.

• Given the recent revisions in society guidelines,1–9 lipid management strategy based on the 10-year ASCVD risk, rather than a particular LDL-C target value, should be implemented in future trials.

RESULTS

Figure 2

A 24-week treatment with aldamer improves liver histology in NASH patients with paired liver biopsies. Aldafermin treatment was effective in reducing liver fat content, liver enzymes (ALT and AST) and liver histology in patients who were on statin and those who were not on statin (Table 1).

Figure 3

Change in LDL-C from Baseline

Aldafermin produced similar efficacy on liver fat content, liver enzymes (ALT and AST) and liver histology in patients who were on statin and those who were not on statin.

Figure 4

Liver Fat Content

At week 24, patients in the aldamer group had an overall favorable lipid and lipoprotein profile, and an improved 10-year ASCVD risk compared with placebo.

Figure 5

Change in Triglycerides from Baseline

CONCLUSION

• Rosuvastatin can safely manage the cholesterol increase seen in NASH patients treated with aldamer.

• At week 24, patients in the aldamer group had an overall favorable lipid and lipoprotein profile, and an improved 10-year ASCVD risk compared with placebo.

• Given the recent revisions in society guidelines, lipid management strategy based on the 10-year ASCVD risk, rather than a particular LDL-C target value, should be implemented in future trials.

REFERENCES


8. Grady et al., 2019 ASCVD risk score and the Primary Prevention of Cardiovascular Disease.


11. NGM Biopharmaceuticals. Author disclosures on file at AASLD.