Aldafermin (NGM282) Improves APRI, FIB-4 and Other Non-Invasive Measures in Patients with Nonalcoholic Steatohepatitis

INTRODUCTION

• Several inexpensive, simple, commonly used non-invasive tests, such as AST to platelet ratio index (APRI) and FIB-4, can predict liver-related outcomes. 1 Increases in these tests are associated with risk of severe liver disease. 2

• Recently, a 2-step FIB-4 (L30S)Δ ELF (v.9.5) algorithm was proposed for identifying at-risk patients with NASH as a primary care referral pathway. 3

• Aldafermin, an engineered FGF19 analog, 4 reduces liver fat and improves fibrosis and NASH resolution. 5

• Here we report the effect of aldafermin on non-invasive tests in a phase 2 study in patients with NASH and fibrosis.

AIM

To assess the effect of aldafermin on several simple, inexpensive, non-invasive tests.

MATERIAL & METHODS

• This phase 2 trial enrolled 4 cohorts of patients with NASH

• In Cohort 1, 82 patients were randomized to aldafermin 3 mg (n=27) or placebo (n=55) for 24 weeks. 6

• In Cohorts 2-3, 94 patients received open-label aldafermin 0.3 mg (n=23), 1 mg (n=49) or 3 mg (n=22) for 12 weeks for dose-ranging finding. 7

• In Cohort 4, 78 patients were randomized to aldafermin 1 mg (n=53) or placebo (n=25) for 24 weeks. 8

Key inclusion criteria included biopsy-proven NASH with NAS >4 (at least 1 point present in each component). Stage 3-4 fibrosis and absolute serum fat content (LFC) by MRI-PDFF ≥20%

APRI, FIB-4, fatty liver index (FLI) and ratio of triglyceride and HDL (TG/HDL) were evaluated at baseline and post treatment.

RESULTS

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

• In Cohort 6, liver biopsy evaluation was performed at baseline and week 24 in patients receiving aldafermin 1 mg or placebo. At-risk patients were identified using the primary care referral pathway. 9

• In this at-risk population, a greater proportion of patients in the aldafermin group achieved fibrosis improvement and NASH resolution compared with placebo.

CONCLUSION

• Aldafermin therapy produced improvements in several simple and inexpensive non-invasive tests of liver fibrosis, steatosis and cardiovascular risk.

• Among at-risk patients identified by non-invasive tests, a greater proportion of patients in the aldafermin group achieved fibrosis improvement and NASH resolution compared with placebo.

REFERENCES


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