



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



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INTRODUCTION

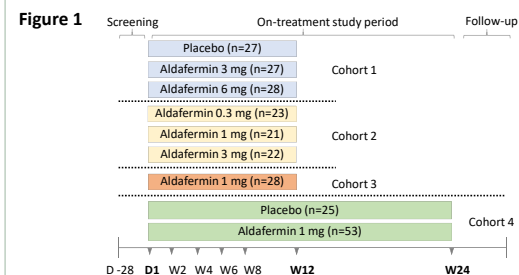
- Several inexpensive, simple, commonly used non-invasive tests, such as AST to platelet ratio index (APRI) and FIB-4 index, can predict liver-related outcomes¹. Increases in these tests are associated with risk of severe liver disease²
- Recently, a 2-step FIB-4 (≥1.30)±ELF (>9.5) algorithm was proposed for identifying at-risk patients with NASH as a primary care referral pathway³
- Aldafermin, an engineered FGF19 analog⁴⁻⁵, reduces liver fat and improves fibrosis and NASH resolution⁶⁻⁹
- 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 3mg (n=27) or 6mg (n=28) vs. placebo (n=27) as a daily SC injection for 12 weeks⁶
- In Cohorts 2-3, 94 patients received open-label aldafermin 0.3mg (n=23), 1mg (n=49) or 3mg (n=22) for 12 weeks for dose-range finding⁷⁻⁸
- In Cohort 4, 78 patients were randomized to aldafermin 1mg (n=53) or placebo (n=25) for 24 weeks⁹
- 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 and post treatment



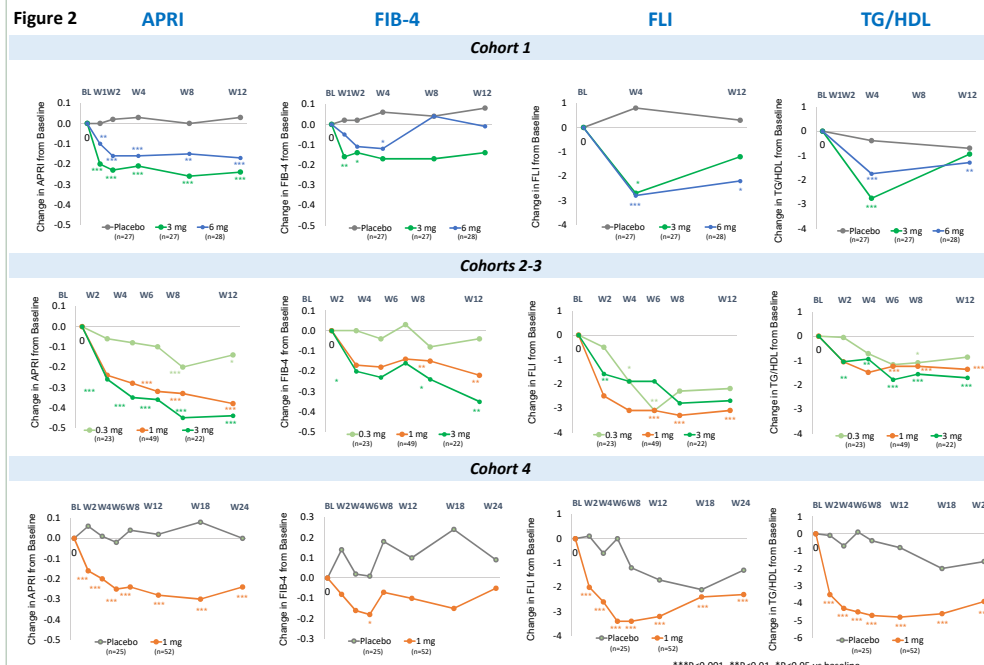
RESULTS

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

Table 1 Baseline Non-invasive Test Values

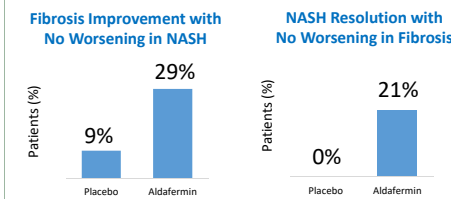
	APRI	FIB-4	FLI	TG/HDL
Cohort 1				
PBO (n=27)	0.73 (0.40)	1.67 (0.79)	87.7 (13.7)	5.10 (5.50)
Aldafermin 3mg (n=27)	0.66 (0.49)	1.54 (0.78)	84.6 (11.6)	5.82 (5.31)
Aldafermin 6mg (n=28)	0.49 (0.28)	1.33 (0.55)	84.0 (23.2)	4.31 (2.65)
Cohorts 2-3				
Aldafermin 0.3mg (n=23)	0.66 (0.41)	1.18 (0.49)	89.4 (13.4)	4.50 (4.03)
Aldafermin 1mg (n=49)	0.73 (0.42)	1.47 (0.65)	91.4 (8.7)	3.82 (1.82)
Aldafermin 3mg (n=22)	0.79 (0.39)	1.72 (0.68)	95.2 (7.5)	4.00 (2.10)
Cohort 4				
PBO (n=25)	0.50 (0.27)	1.36 (0.57)	88.0 (13.7)	7.00 (8.90)
Aldafermin 1mg (n=53)	0.71 (0.41)	1.71 (1.02)	89.7 (12.9)	8.50 (12.91)

- Aldafermin-treated patients showed robust and persistent reductions in non-invasive tests of fibrosis (APRI and FIB-4), fatty liver (FLI), and cardiovascular risk (TG/HDL ratio)



- In Cohort 4, 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 pathway³
- In this at-risk population, a greater proportion of patients in the aldafermin group achieved fibrosis improvement and NASH resolution compared with placebo

Figure 3



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

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