Atherosclerotic Cardiovascular Risk Assessment in a 24-Week, Randomized, Double-Blind, Placebo-Controlled Study of Aldafermin

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INTRODUCTION

• Non-alcoholic steatohepatitis (NASH) is associated with an increased risk of cardiovascular disease 1.
• Recent society guidelines recommend initiating statins in patients with elevated cardiovascular risk 2-4.

AIM

To assess changes in the 10-year atherosclerotic cardiovascular disease risk score (ASCVD) and atherogenic lipoproteins in a 24-week study of aldafermin in patients with NASH.

METHOD

• 78 subjects were randomized 1:2 to receive placebo (n=25) or aldafermin 1 mg (n=53) SC QD for 24 weeks.
• Key inclusion criteria included biopsy-confirmed NASH with NAS≥4, stage 2-3 fibrosis and absolute liver fat content ≥8%.

RESULTS

• At baseline, mean 10-year ASCVD risk scores were 15.0% and 11.6% in the aldafermin and placebo groups, respectively.
• At week 24, a greater reduction from baseline in the ASCVD risk score was observed in the aldafermin group compared to placebo (−3.4% and −1.2% in absolute ASCVD score in aldafermin and placebo groups, respectively, P=0.032 vs placebo).

AIM

• Aldafermin is an engineered FGF19 analogue that inhibits bile acid synthesis and regulates metabolic homeostasis 5.

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

• Here we report results on cardiovascular risk assessment and key lipoproteins implicated in atherosclerosis from this study.

CONCLUSIONS

• Aldafermin-associated cholesterol increase can be safely managed with a statin.
• At the end of treatment, a greater reduction in the 10-year ASCVD risk score was achieved in the aldafermin group compared with placebo.
• Patients in the aldafermin group had lower triglyceride and cholesterol content in TRL, lower levels of proatherogenic lipoprotein ApoB, and higher levels of the anti-atherogenic lipoprotein ApoA1 at week 24.
• Patients in the aldafermin group, but not the placebo group, had significant reductions in the pro-atherogenic lipoprotein ApoB (−11.0%, P=0.037 vs baseline).
• However, aldafermin increased serum cholesterol levels by inhibiting CYP7A1, which encodes the rate-limiting enzyme in the conversion of cholesterol to bile acids.

REFERENCES


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