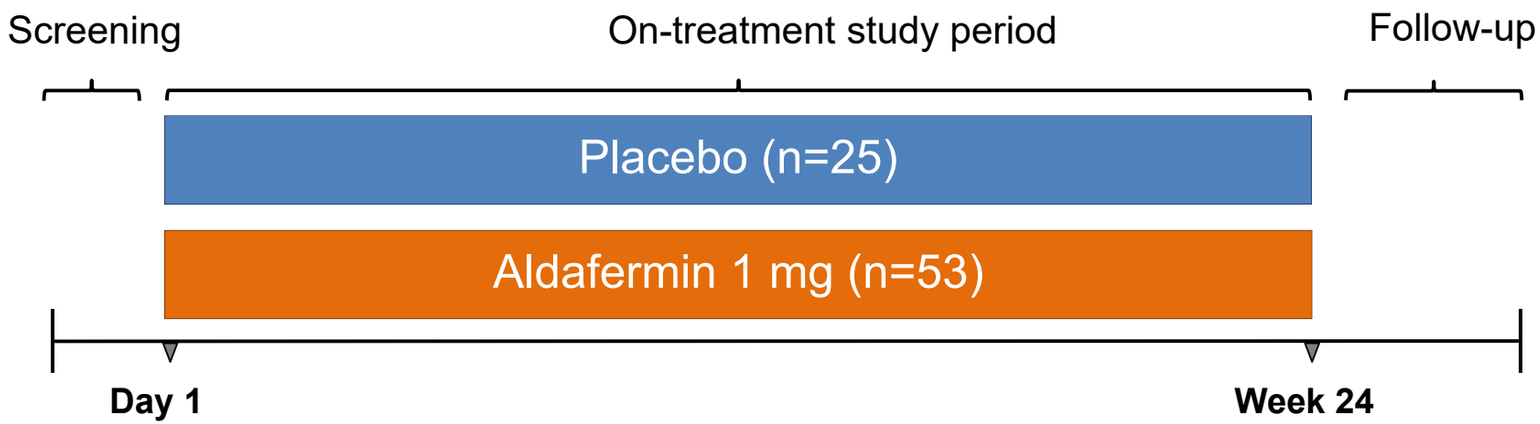
Atherosclerotic Cardiovascular Risk Assessment in a 24-Week, Randomized, Double-Blind, Placebo-Controlled Study of Aldafermin

- Aldafermin (NGM282) is an engineered FGF19 analogue that inhibits bile acid synthesis and regulates metabolic homeostasis [1]
- In a 24-week, randomized, double-blind, placebo-controlled study in NASH patients with serial liver biopsies, aldafermin treatment resulted in liver fat reduction, fibrosis improvement and NASH resolution [2]
- Here we report results on cardiovascular risk assessment and key lipoproteins implicated in atherosclerosis from this study

Population:
NASH, F2 or F3, NAS ≥4, MRI-PDFF ≥8%

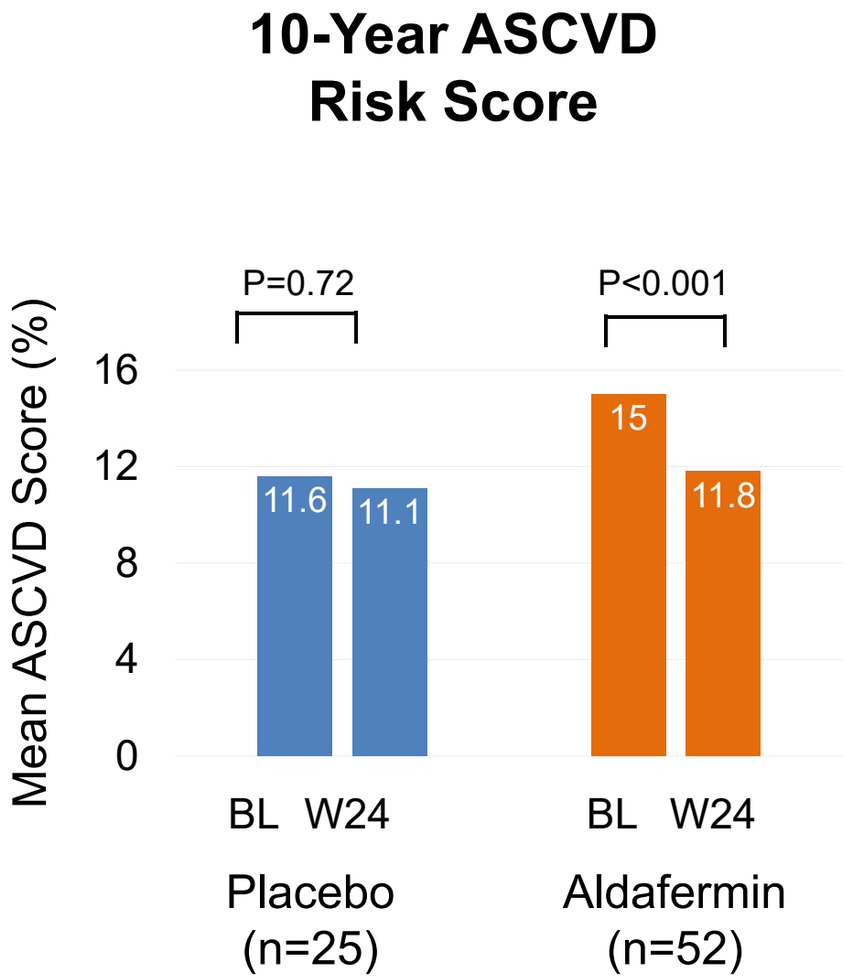
Lipid management:
As pre-specified in the protocol, subjects were to start with rosuvastatin if statin naïve or switch to rosuvastatin if already on statin therapy, to treat LDL-C elevations of >10 mg/dL from baseline [3]

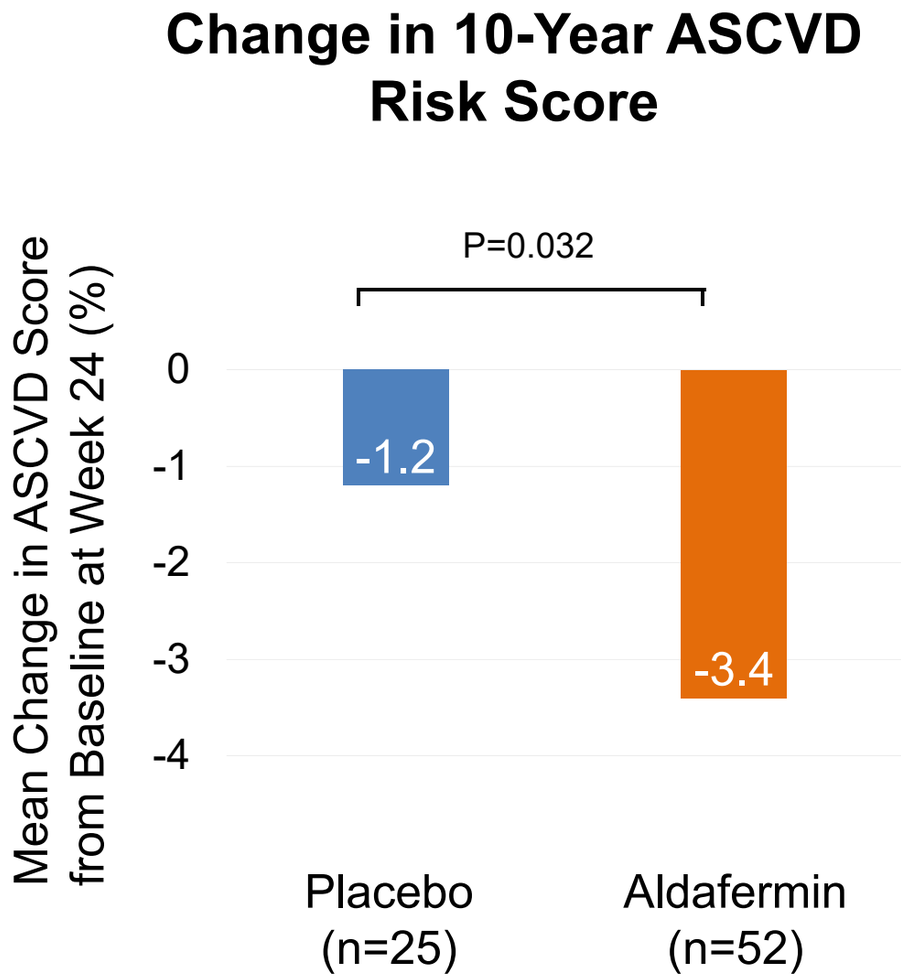


Gunn et al., Abstract 1082 (EASL 2021)

[1]DePaoli et al., Diabetes 2019;68:1315-1328; [2]Harrison et al., Gastroenterology 2021;160:219-231; [3]Gunn, AASLD 2020

10-Year ASCVD Risk Score Was Reduced in the Aldafermin Group Compared to Placebo at Week 24





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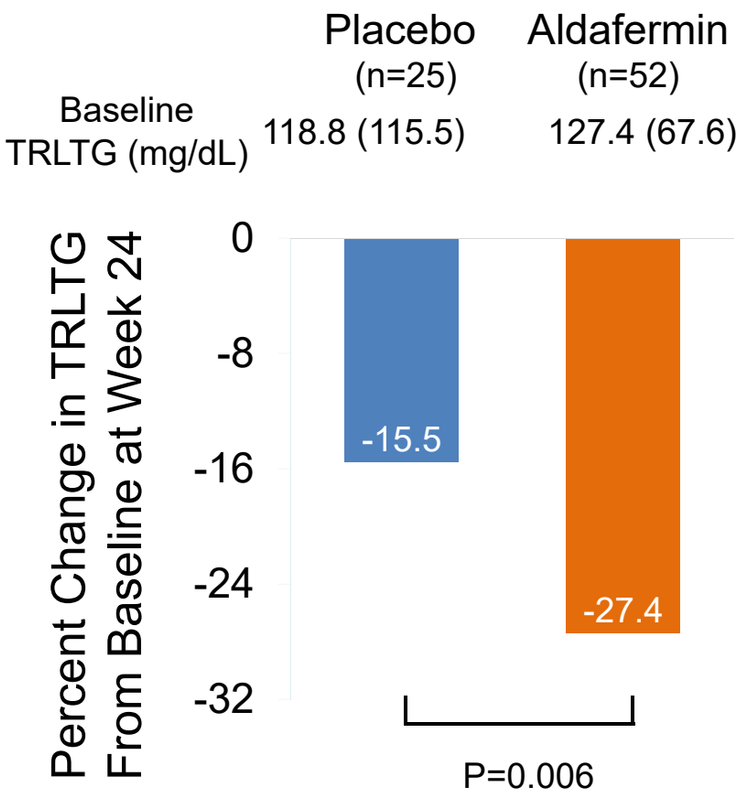
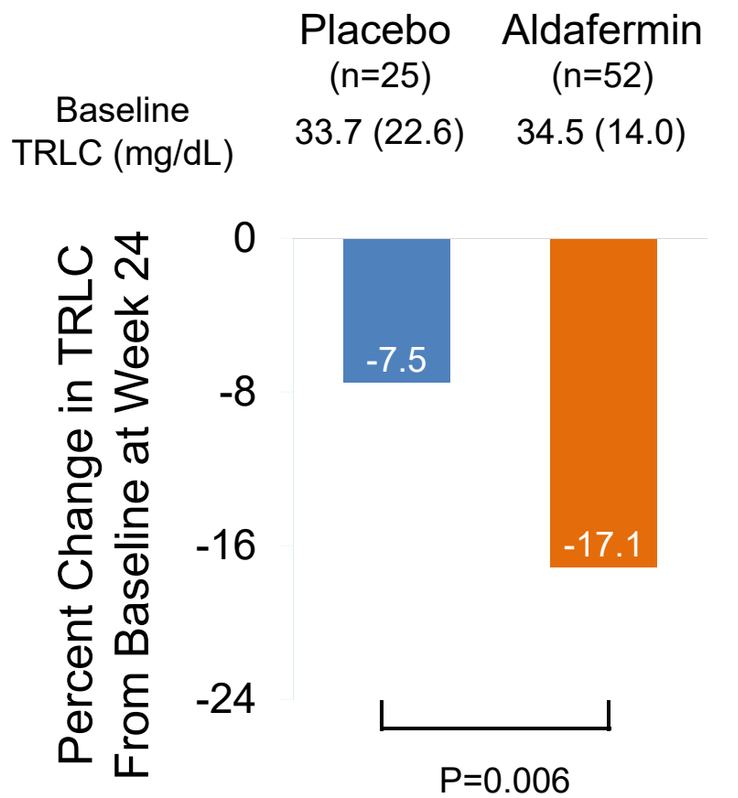
10-year atherosclerotic cardiovascular disease (ASCVD) risk calculator at: http://tools.acc.org/ASCVD-Risk-Estimator

Both Triglyceride Content and Cholesterol Content in the TRLs Were Lower in the Aldafermin Group versus Placebo at Week 24

TRL Triglyceride Content



TRL Cholesterol Content



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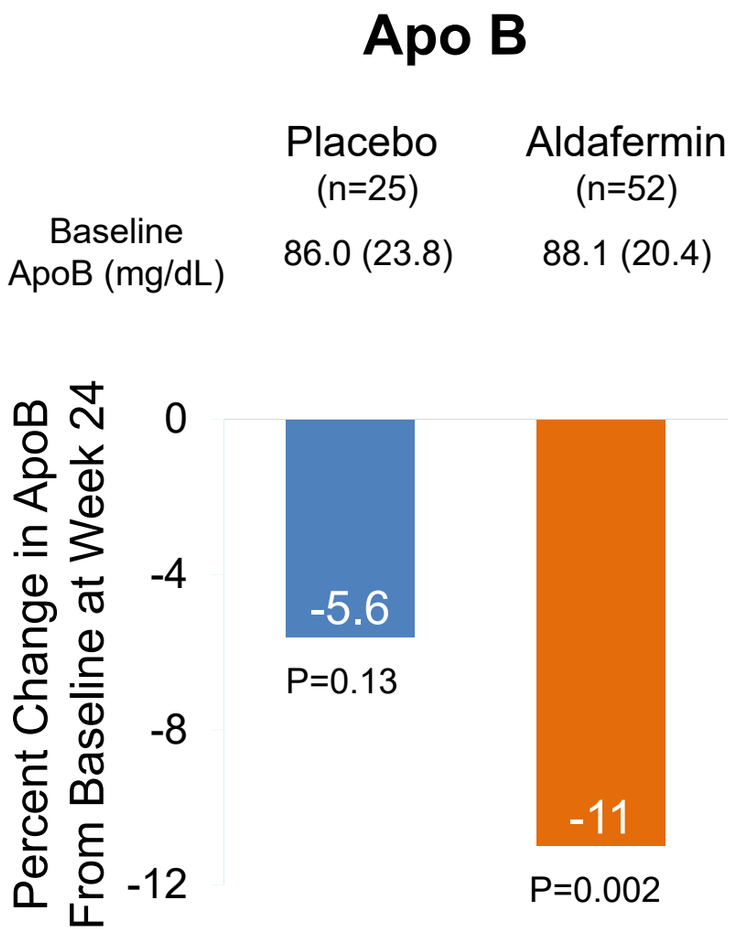
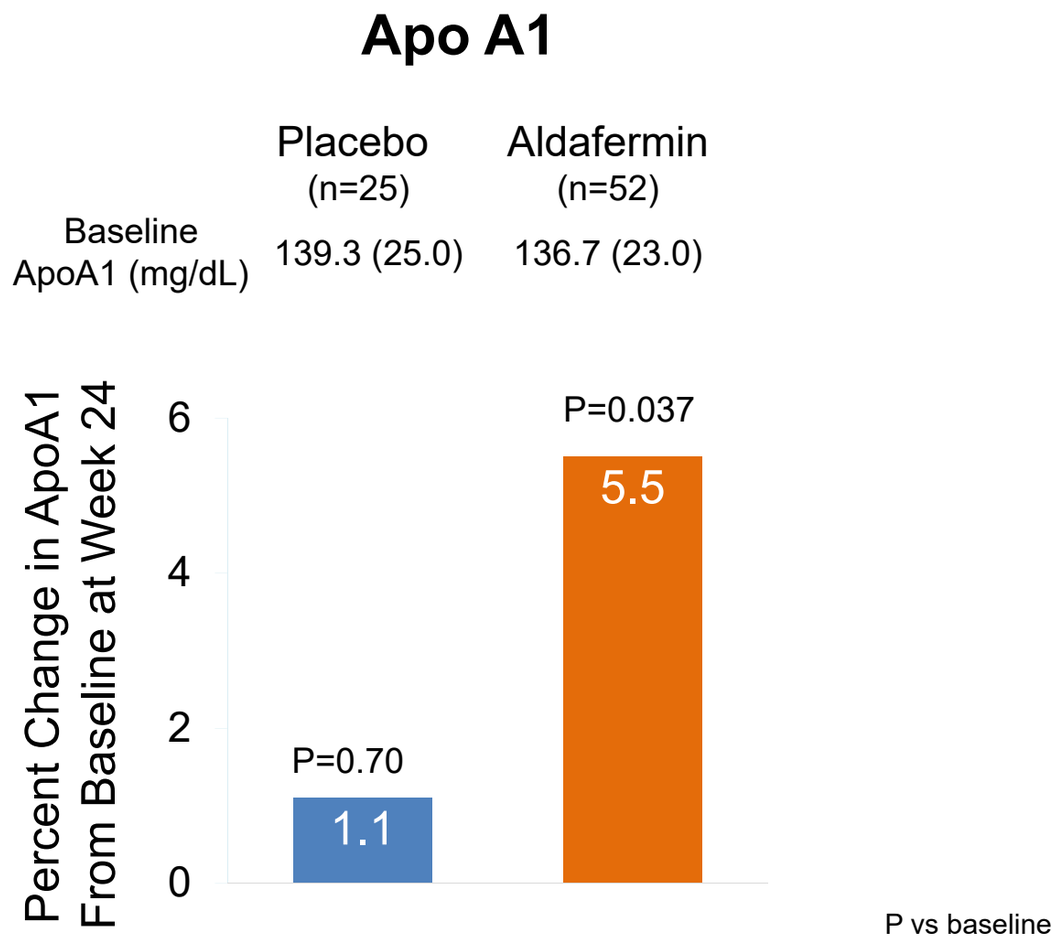
TRL, triglyceride-rich lipoproteins; TRLTG, TRL triglyceride content; TRLC, TRL cholesterol content

Reduction of the Pro-Atherogenic Lipoprotein ApoB and Increase of the Anti-Atherogenic Lipoprotein ApoA1 in the Aldafermin Group





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Conclusion

- 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 pro-atherogenic 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 reductions from baseline in lipoprotein insulin resistance index at week 24
- In this study in patients with NASH and fibrosis, an overall favorable cardiovascular risk profile was achieved in the aldafermin arm

Acknowledgment

- We thank all of the patients who participated in this study, and the investigators, study coordinators and staff for their support