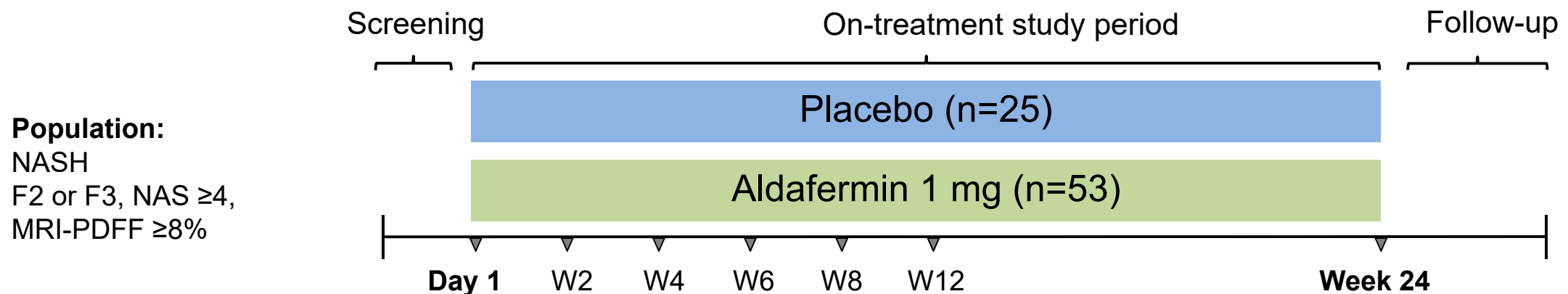


Aldafermin Reduces Hydrophobic Bile Acids in a 24-Week, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study in Patients with Nonalcoholic Steatohepatitis



- Higher serum bile acid levels are associated with an increased risk of cirrhosis and liver-related morbidity and mortality ¹
- Serum bile acids correlate with portal hypertension, and can predict decompensation, liver failure and transplant-free survival in chronic liver disease ¹
- Aldafermin, an engineered FGF19 analog, potently inhibits bile acid synthesis via the suppression of CYP7A1, which encodes the first and rate-limiting enzyme in the classic bile acid synthetic pathway ²
- Here we report results from a secondary analysis of aldafermin on circulating bile acid profile in a 24-week, randomized, double-blind, placebo-controlled trial in patients with NASH

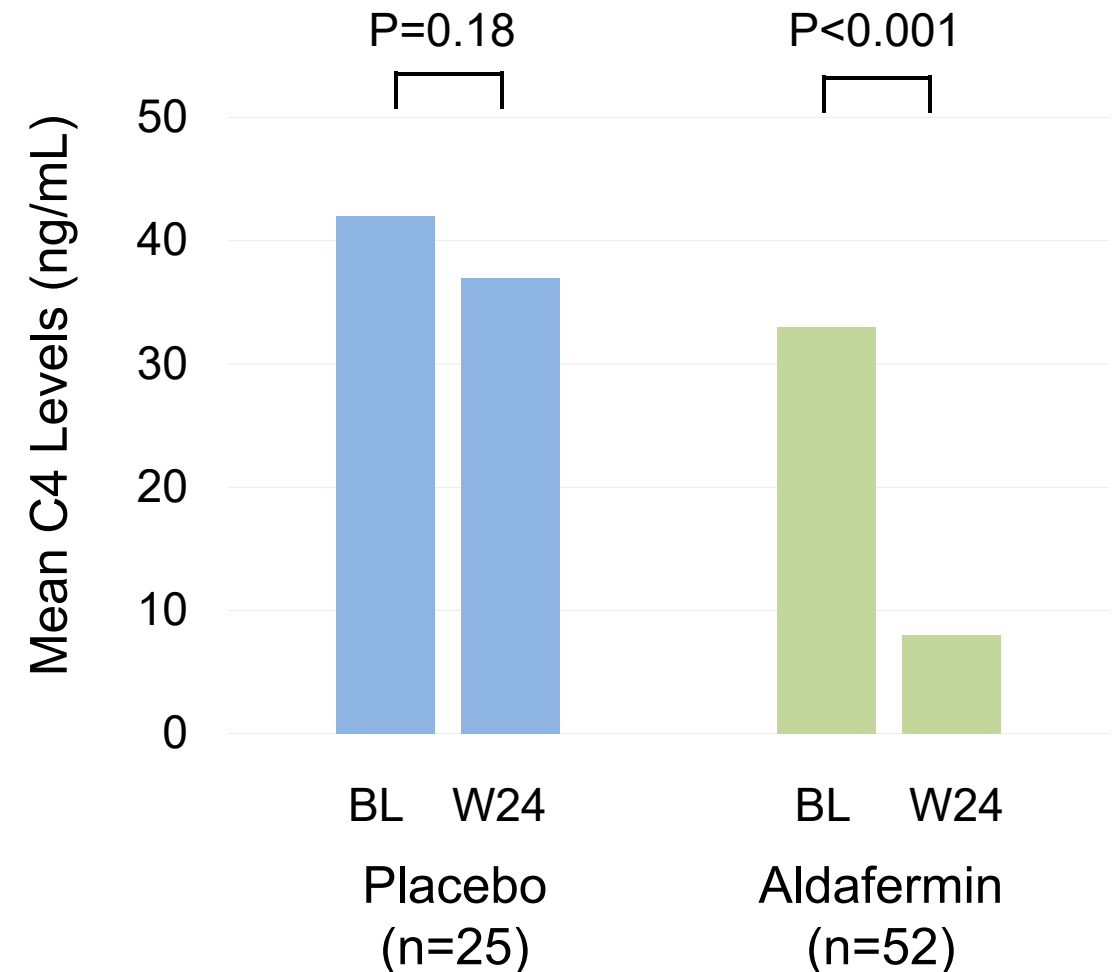


Robust Reduction of 7alpha-Hydroxy-4-Cholesten-3-One, A Surrogate of Bile Acid Synthesis, by Aldafermin

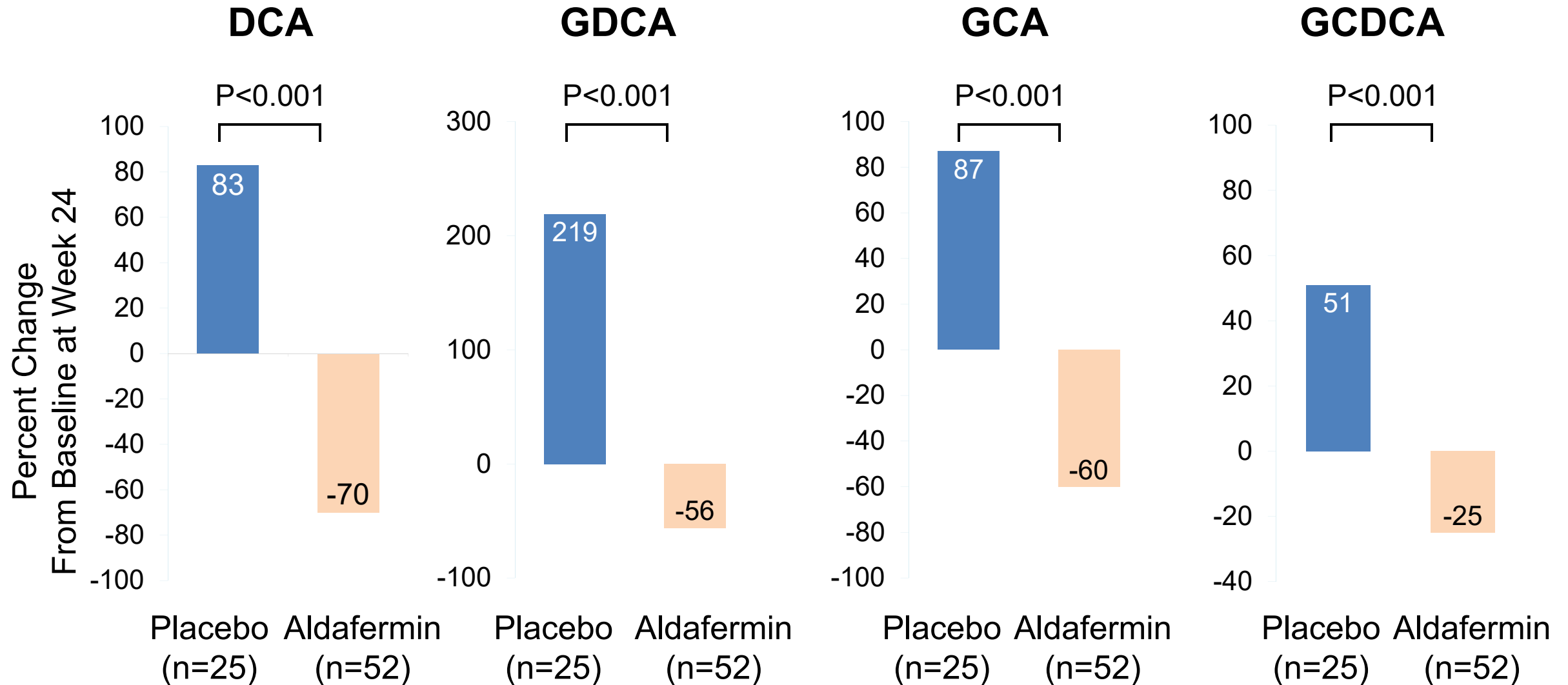


- Serum level of 7alpha-hydroxy-4-cholesten-3-one (C4), a surrogate of hepatic CYP7A1 activity, is a pharmacodynamics marker of aldafermin activity
- At week 24, a greater reduction from baseline in C4 was observed in the aldafermin group compared to placebo (P<0.001)

7alpha-hydroxy-4-cholesten-3-one

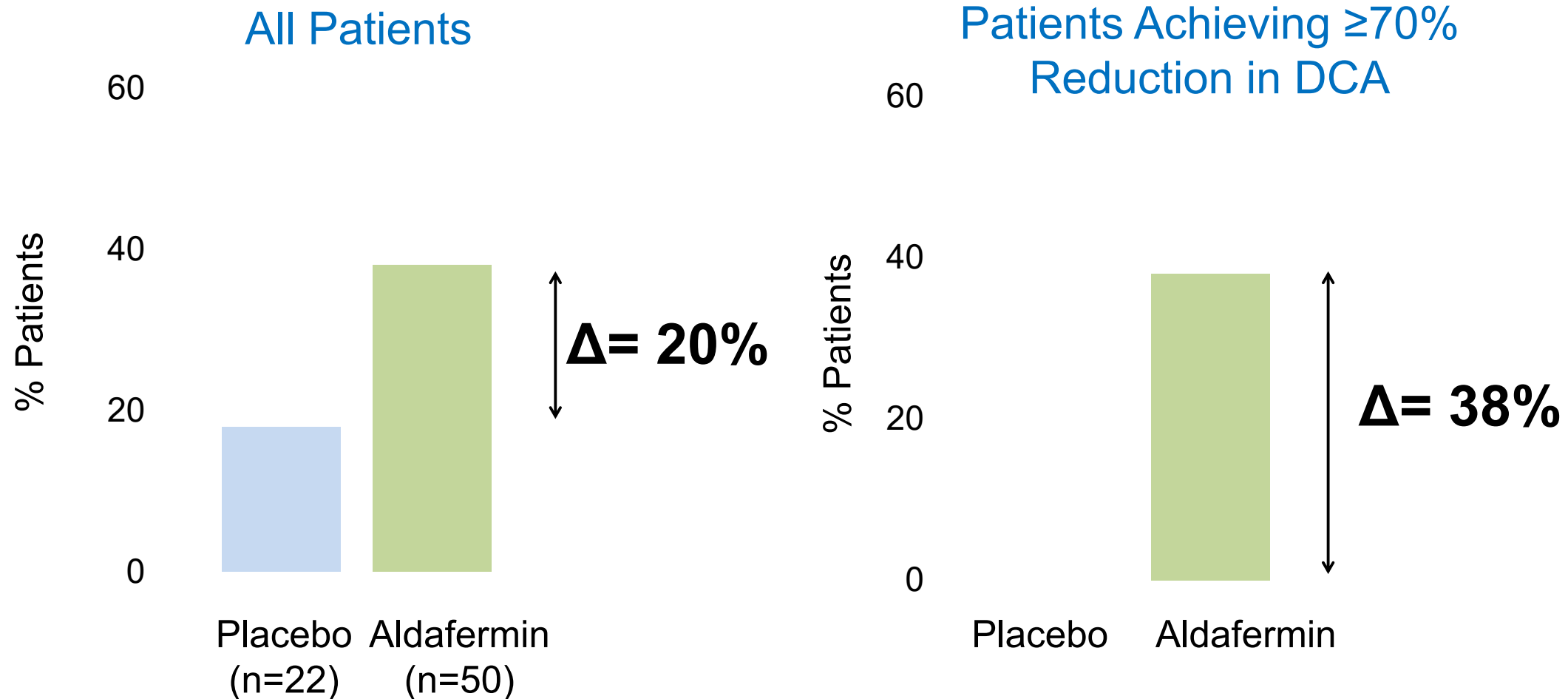


Aldafermin Treatment Produced Marked Reductions in Hydrophobic Bile Acids, and DCA in Particular



Greater Anti-Fibrotic Effects with Aldafermin in Patients Who Achieved $\geq 70\%$ Reduction in DCA

Fibrosis Improvement (≥ 1 -stage) with No Worsening in NASH ¹



Conclusion



- Administration of aldafermin produced significant reductions in bile acids, and the more toxic, hydrophobic bile acids in particular
- Among individual bile acids, aldafermin generated the most robust reduction in the secondary bile acid DCA
- The preferential reduction of the more hydrophobic, glycine-conjugated bile acids, rather than the more hydrophilic, taurine-conjugated, bile acids by aldafermin resulted in a lower G/T ratio and reduced bile acid toxicity
- Aldafermin had greater anti-fibrotic effects in patients who achieved $\geq 70\%$ reduction in DCA
- Results from this 24-week study in an independent cohort confirm and validate previous findings from 12-week studies ¹

Acknowledgment

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