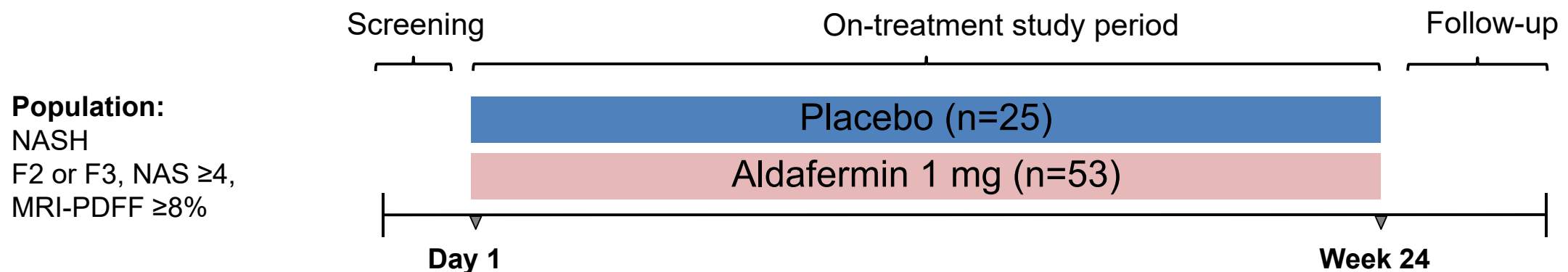


The Liver Fibroinflammatory Marker cT1 is Reduced with Aldafermin Therapy in a Randomized, Double-Blind, Placebo-Controlled, Multicenter Study in Patients with Nonalcoholic Steatohepatitis



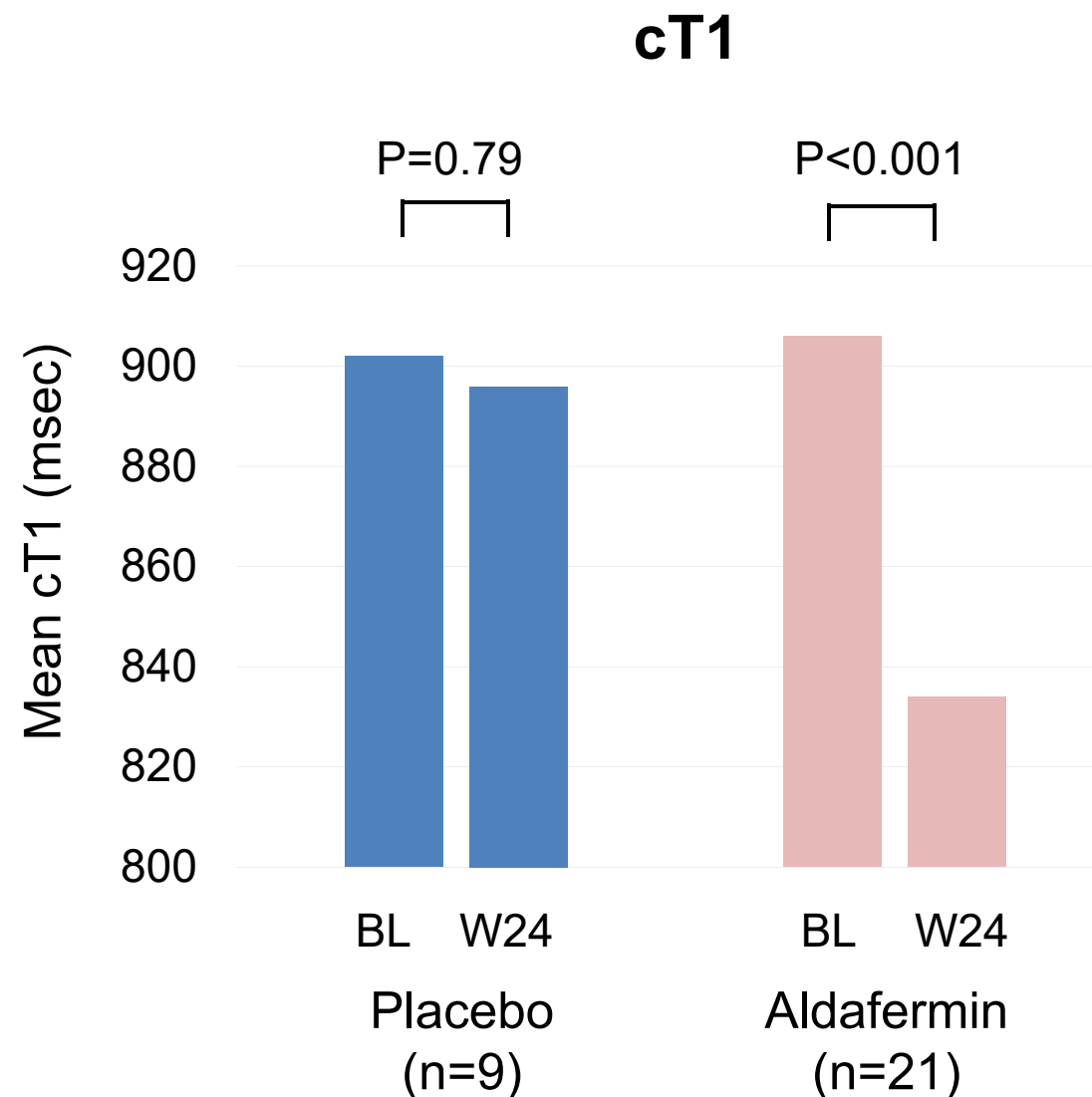
- The iron-corrected T1 relaxation time (cT1) is a novel imaging marker of intrahepatic fibro-inflammatory activity and is used in the UK Biobank population health study as the reference for liver fibroinflammatory disease
- A threshold of cT1 >825ms has been shown to predict clinical outcomes (ascites, variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma, liver transplantation, mortality; hazard ratio of 9.9, P=0.007) ¹
- Aldafermin, an engineered FGF19 analog, produced fibrosis regression and NASH resolution in a 24-week, randomized, double-blind, placebo-controlled trial in patients with NASH ²
- Here we report the effect of aldafermin on the novel imaging marker cT1 in this trial



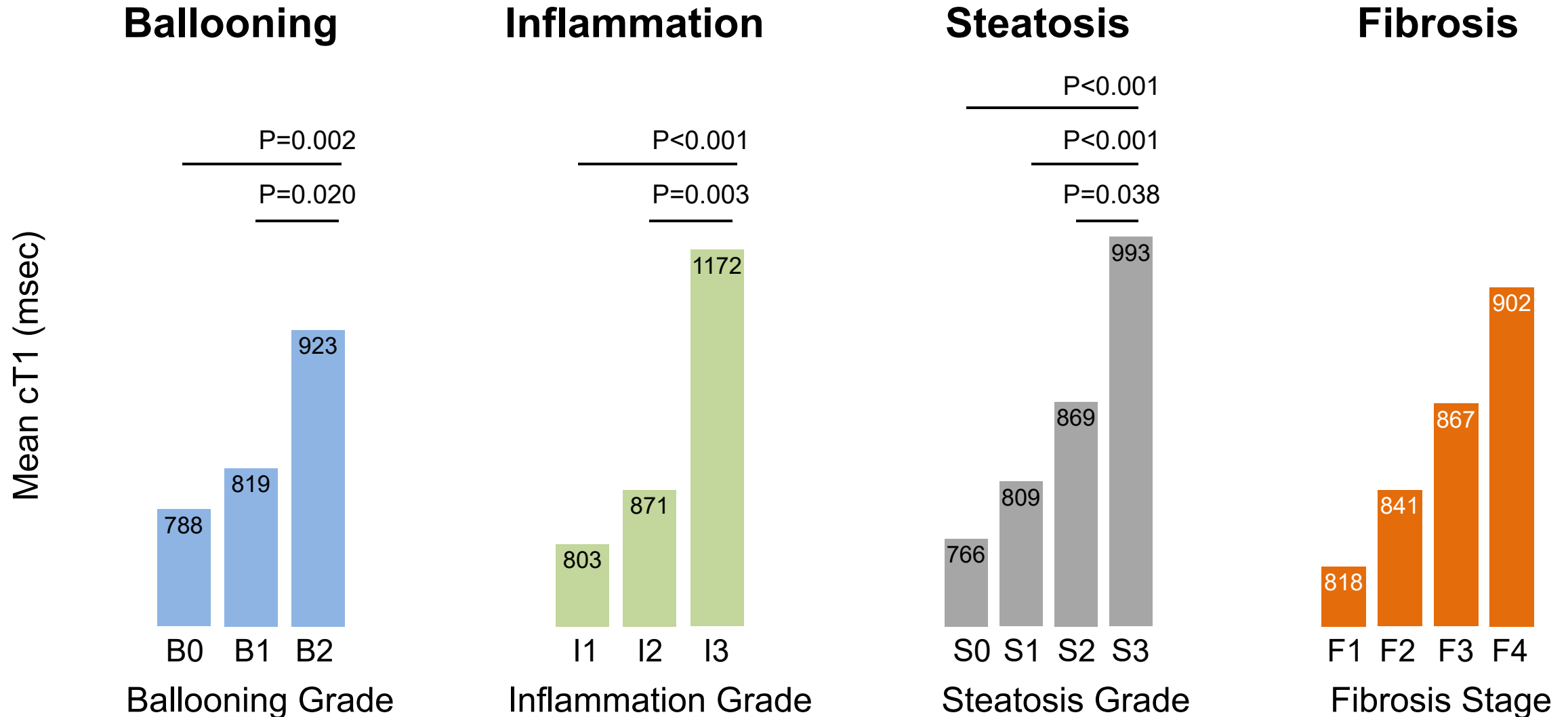
Aldafermin Demonstrated Significant Reductions in cT1 Compared to Placebo



- cT1 maps were analyzed by trained central readers blinded to treatment assignment, clinical and histological information
- Because LiverMultiScan™ (Perspectum Diagnostics, UK) was not available at some study sites, overall 30 patients (9 and 21 in the placebo and aldafermin groups, respectively) had evaluable cT1 maps at both baseline and week 24 and were included in this analysis
- At week 24, cT1 values declined significantly in aldafermin-treated subjects. In contrast, no change in cT1 was observed in placebo-treated subjects (difference in LS mean, -86 msec, $P=0.03$ vs placebo)



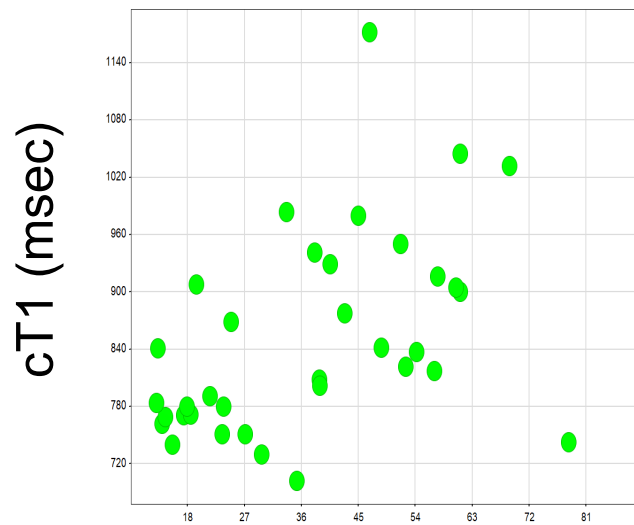
cT1 Correlated with Histological Grades of Ballooning, Inflammation and Steatosis at Week 24



cT1 Correlated with Serum Markers of Liver Injury and Fibrosis at Week 24

ALT

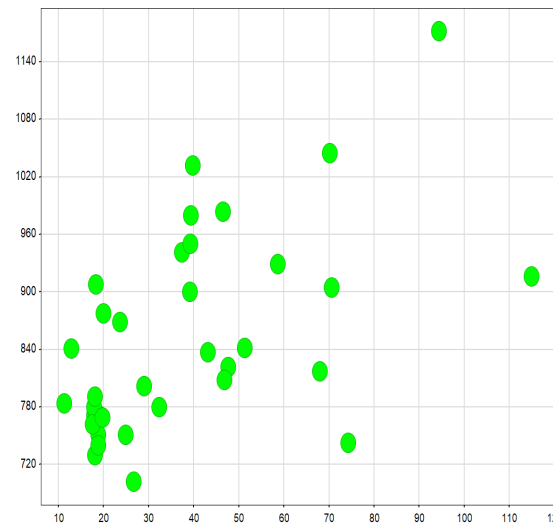
$\rho = 0.51$
 $P = 0.002$



ALT
(U/L)

AST

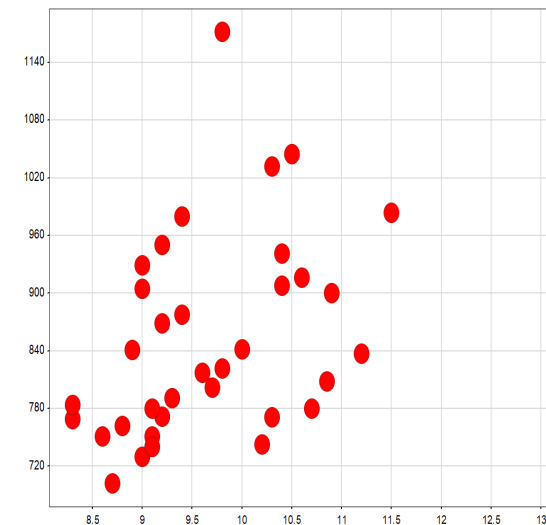
$\rho = 0.53$
 $P = 0.001$



AST
(U/L)

ELF

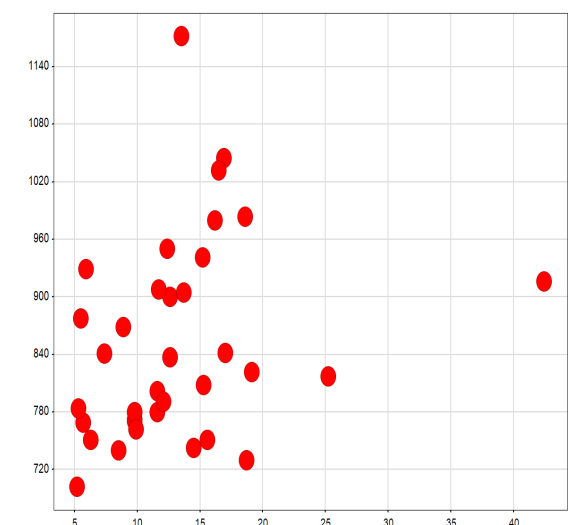
$\rho = 0.48$
 $P = 0.004$



ELF

Pro-C3

$\rho = 0.37$
 $P = 0.027$



Pro-C3
(ng/mL)

Conclusion

- Compared to placebo, aldafermin demonstrated significant reductions in cT1 values, consistent with its anti-inflammatory and anti-fibrotic effect on the NASH liver
- cT1 correlated with histological grades of ballooning, inflammation and steatosis, as well as non-invasive measures including ALT, AST, ELF and Pro-C3, at week 24
- cT1 may be used as a tool to follow patients over time to assess response to treatment and disease progression
- Given the prognostic value of cT1 on clinical outcomes, aldafermin treatment may provide benefits to the at-risk patient population defined as having cT1 >825ms

Acknowledgment

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