Efruxifermin is Associated With Improved Glucose Metabolism in Patients With NASH and Type 2 Diabetes

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Disclosures

Research Support: Akero, AbbVie, AstraZeneca, Boehringer Ingelheim, BMS, Eli Lilly, Intercept, Janssen, Madrigal, Metacrine, Merck, NorthSea Therapeutics, Novartis, Novo Nordisk, Oramed, Pfizer, Poxil, Sanofi, Theracos

Advisory Boards and Consultant: Akero, Altimmune, Axcella Health, Boehringer Ingelheim, Carmot, Coherus Therapeutics, Echosens, 89bio, Eli Lilly, Gilead, Intercept, Merck, Novo Nordisk, Pfizer, Sanofi

Speaker Bureau: Eli Lilly, Merck, Sanofi

Background and Aims

- One-third of patients with type 2 diabetes (T2D) are estimated to have NASH, therefore, the ability to further improve glycemic control in this patient population is a desirable attribute for future NASH therapies
- Efruxifermin (EFX) is a long-acting Fc-FGF21 fusion protein being developed as a therapeutic for NASH
- The BALANCED study[1] was a randomized, double-blind, placebo-controlled study in patients with NASH and fibrosis stage 1-3, treated for 16 weeks with once weekly (QW) placebo or EFX 28, 50, or 70 mg
  - QW dosing was supported by a Phase 1b study in T2D[2] where markers of glucose metabolism improved with QW dosing, but not with Q 2-week dosing
- Following 16 weeks of treatment, EFX demonstrated robust reductions in liver fat content (including normalization of liver fat in approximately half of all EFX-treated patients), as well as improvements in markers of liver injury, fibrosis, and lipid and glucose metabolism[1]

The aim of this analysis was to evaluate the effects of EFX on markers of glucose metabolism in patients with NASH and in the subgroup with T2D (N=41).

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[1]Harrison et al 2021. Nature Medicine, *In Press;* [2]Kaufman et al 2020 *Cell Rep Med* 1:100057

Demographics and baseline characteristics

Parameter Mean or %	All Randomized Patients[1] (N=80)	Patients with Type 2 Diabetes[2] (N=41)
Age (Years)	52	54
% Female Sex	58	59
% Hispanic or Latino Ethnicity	50	42
% Type 2 Diabetes	**51**	**100**
HbA1c (%)	**6.34**	**6.96**
Weight (kg)	103.5	104.7
BMI (kg/m^2)	37.56	38.1
% F2 or F3	64	66
Alanine Aminotransferase (ALT) (U/L)	56	54
Aspartate Aminotransferase (AST) (U/L)	40	41
Triglycerides (mg/dL)	186	201
Select Background Medications, %		
Metformin	38	71
Sulfonylureas	13	24
GLP-1 Receptor Agonists	9	15
Lipid-lowering medications (primarily statins)	37	54

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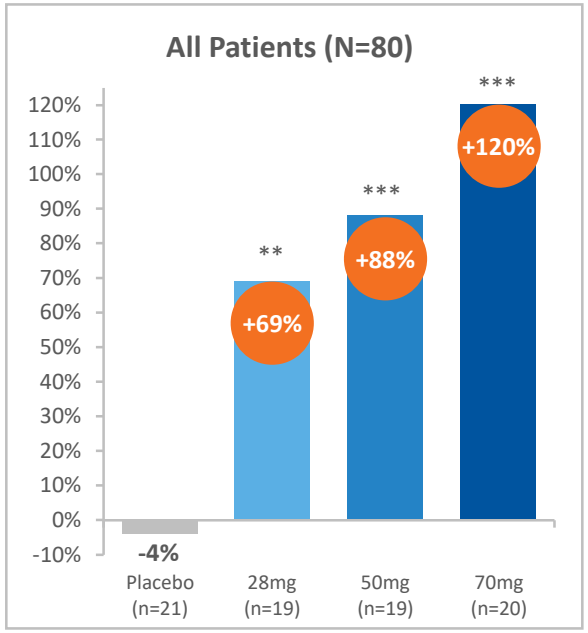
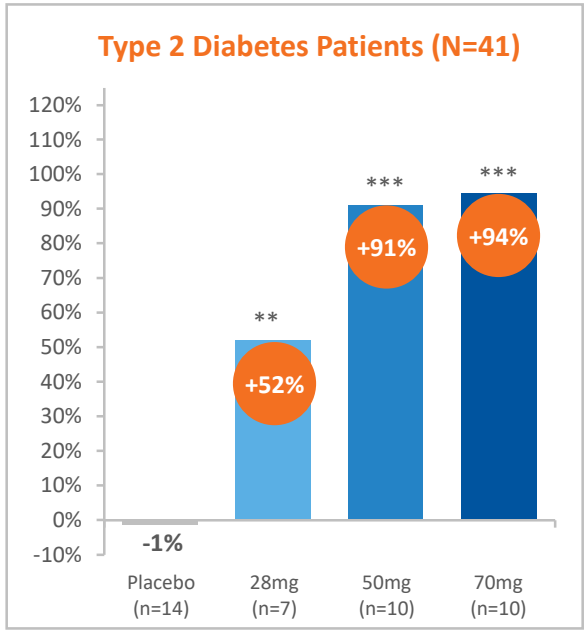
[1] Full Analysis Set, F1-F3 (all subjects randomized into the BALANCED main study); [2] FAS, T2D subgroup

Dose-dependent increases in adiponectin, a pharmacodynamic marker of FGFR1c activation, with efruxifermin

LS Mean Change in Adiponectin From Baseline to Week 16 (%)



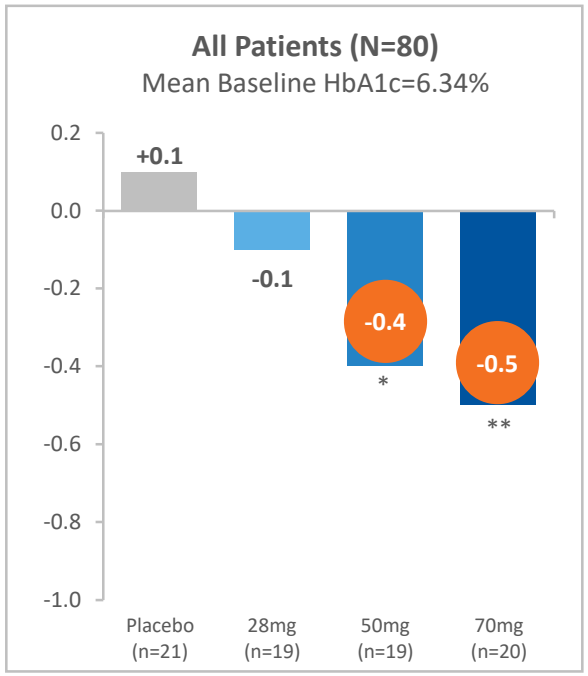
* p<0.05, ** p<0.01, *** p<0.001, versus placebo (ANCOVA)



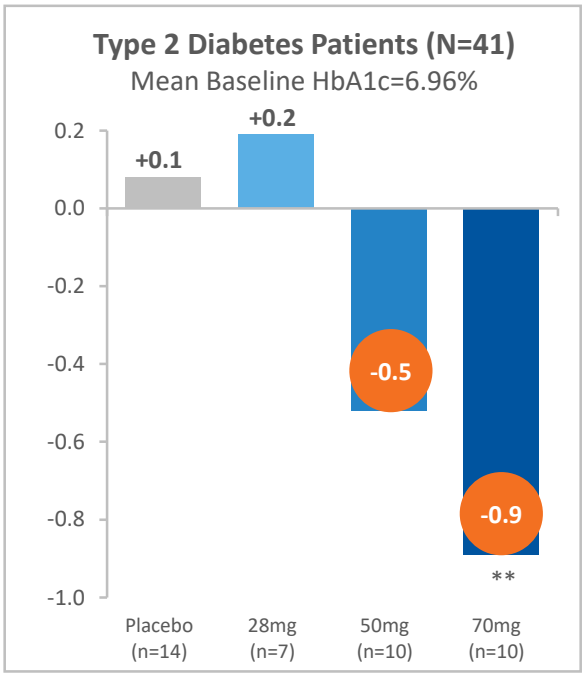
* p<0.05, ** p<0.01, *** p<0.001, versus placebo (ANCOVA)

Dose-dependent improvements in HbA1c with efruxifermin

LS Mean Change in HbA1c From Baseline to Week 16 (%)



* p<0.05, ** p<0.01, versus placebo (ANCOVA)

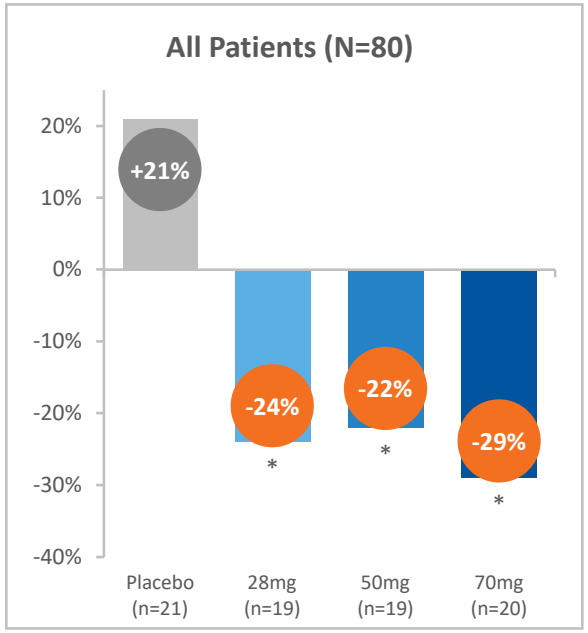


* p<0.05, versus placebo (ANCOVA)

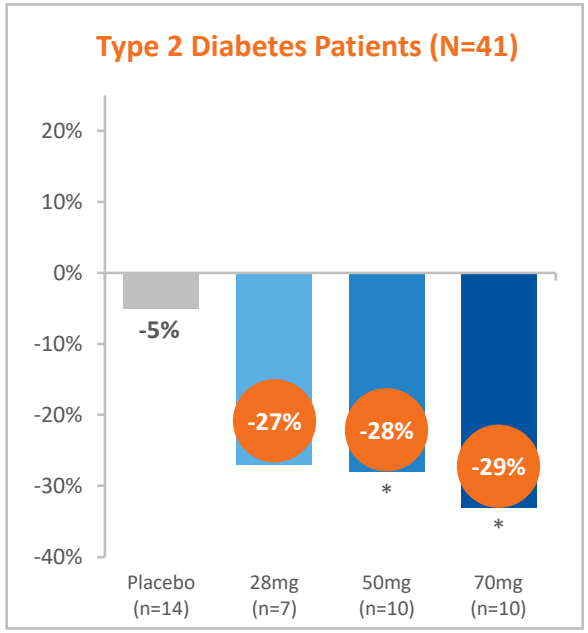
Source Data: Full Analysis Set; FAS Type 2 Diabetes Subgroup

Efruxifermin improved insulin sensitivity

LS Mean Change in C-Peptide From Baseline to Week 16 (%)



* p<0.05, versus placebo (ANCOVA)

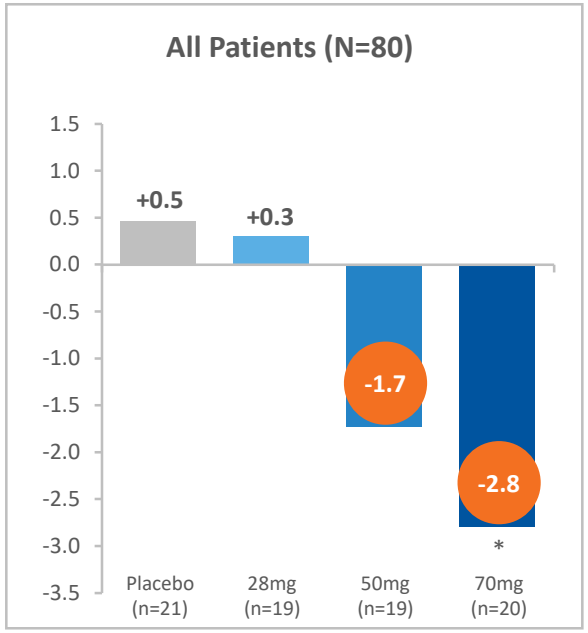


* p<0.05, versus placebo (ANCOVA)

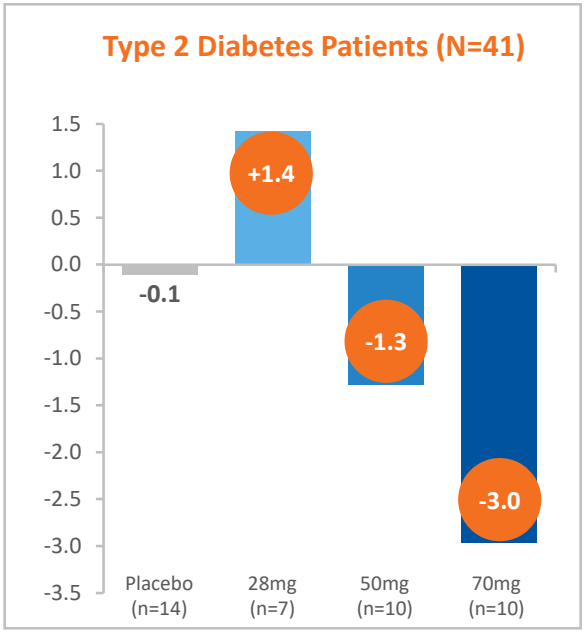
Source Data: Full Analysis Set; FAS Type 2 Diabetes Subgroup

Change in body weight following treatment with efruxifermin

LS Mean Change in Body Weight From Baseline to Week 16 (%)



* p<0.05, versus placebo (ANCOVA)

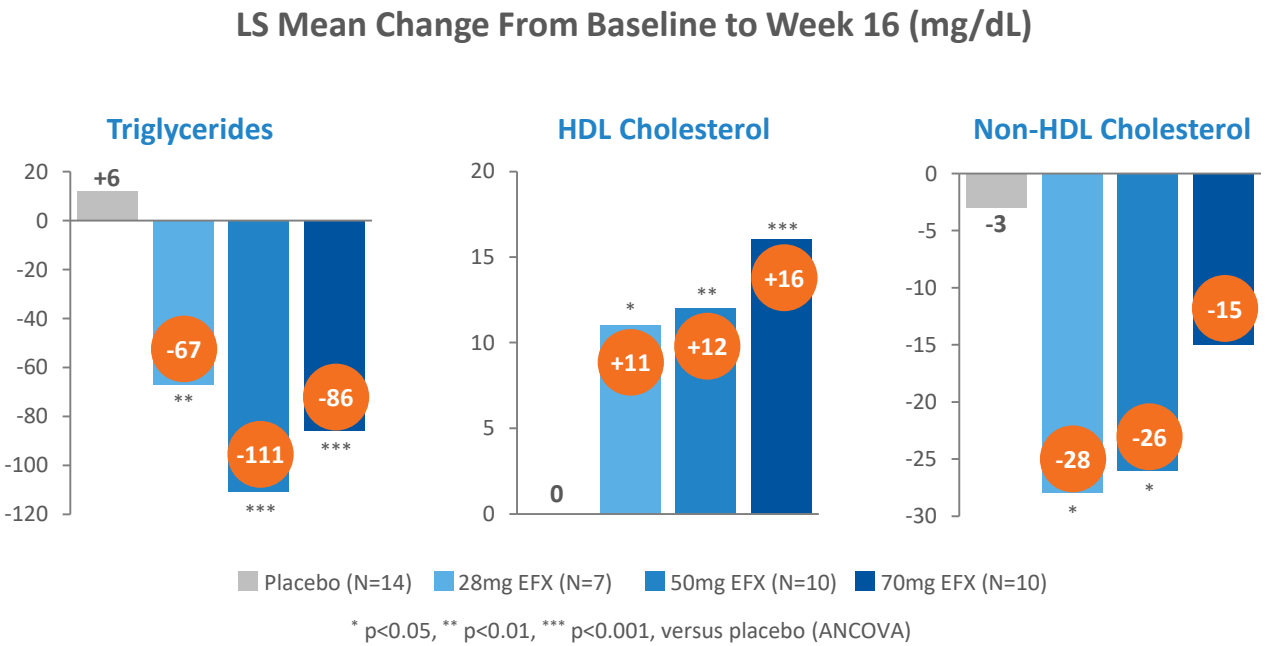


* p<0.05, versus placebo (ANCOVA)

- EFX enhanced insulin sensitivity without gain in body weight, and rather, demonstrated a trend for reduction in body weight

Source Data: Full Analysis Set; FAS Type 2 Diabetes Subgroup

Efruxifermin improved lipoprotein profile



- EFX restored a healthy lipid profile in NASH patients with T2D

Summary and Conclusions

SUMMARY

- Half of the NASH patients with F1-F3 fibrosis randomized in BALANCED study had T2D
  - >70% of T2D patients were on metformin and ~15% were on GLP-1 receptor agonists

- Following 16 weeks of treatment, EFX resulted in:
  - Reduction in HbA1c
  - Improvement in insulin sensitivity
  - Trend to reduce body weight
  - Improved lipoprotein profile

- Safety profile of the T2D subgroup was comparable to that of the overall study population[1]
  - The most frequent treatment emergent adverse events were mild to moderate GI events
  - Two patients on EFX 70 mg experienced Grade 1 hypoglycemia
  - One patient with T2D had an SAE of acute pancreatitis and was discontinued from the study

CONCLUSIONS: Once-weekly EFX (28 to 70 mg) improved markers of glucose control, insulin sensitivity, and lipoprotein profile in patients with NASH and type 2 diabetes following 16 weeks of treatment.

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[1]Harrison et al 2021. Nature Medicine, *In Press*