Characterization of Histologic Patterns of Improvement Following Treatment With Efruxifermin (EFX) in NASH Patients With Fibrosis

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INTRODUCTION

• Efruxifermin (EFX) is a long-acting FGF21 agonist being developed as a potential therapy for patients with NASH and fibrosis.

• In the phase 2a BALANCED study1 in patients with biopsy-confirmed NASH (F1-3), EFX treatment resulted in:
  - 48%–72% relative reduction in liver fat content (LFC) at Week 12
  - Normalization of liver fat (LFC) in 40% of patients
  - Improvement in Sereno-Style Liver Fibrosis Following 24 weeks of treatment:
    - Fibrosis improvement by ≥1 stage in 48% of patients
    - Improvement in 48% of patients
    - Improvement in non-alcoholic fatty liver disease (NAFLD) Activity Score (NAS) by ≥1 at ≥18 weeks

• In Akero’s Ph2b studies, HARMONY (F2/3) and SYMMETRY (F4), evaluating improvement in fibrosis after EFX treatment for 24 and 36 weeks, respectively, will determine if longer treatment durations increase response rates by categorical analysis.

• Most EFX-treated patients with end-of-treatment biopsies showed improvements in features of steatohepatitis (35 of 40; 87%) and/or fibrosis (32 of 40; 80%), after only 16 weeks:


METHODS

• At baseline, all patients had biopsy-confirmed NASH (F2-F3) with NAS ≥4.

• End-of-Study Biopsies were available for 40 EFX-treated patients, all of whom achieved ≥30% relative reduction in LFC on MRI.

• All pre- and post-treatment biopsies were reviewed by a single pathologist blinded to treatment and sequence.

• Post hoc analysis of the recorded histopathology revealed distinct patterns of regression which were classified qualitatively.


RESULTS: STEATOHEPATITIS RESOLUTION CATEGORIES

Table 1. Baseline Characteristics by Extent of Steatohepatitis Resolution

Table 2. Histological Outcomes and Improvements in Biomarkers of Liver-Health Following EFX Treatment by Categories of Steatohepatitis Resolution

Table 3. Baseline Characteristics by Categories of Fibrosis Regression

Table 4. Histological Outcomes and Improvements in Biomarkers of Liver-Health Following EFX Treatment by Categories of Fibrosis Regression

CONCLUSIONS

• Most EFX-treated patients with end-of-treatment biopsies showed improvements in features of steatohepatitis (30 of 40; 87%) and/or fibrosis (32 of 40; 80%), after only 16 weeks:

  1. Improvement in histologic characteristics of steatohepatitis, changes in histologic pattern relative to individual features, and intra-stage histologic changes in fibrosis may be an early indication of response after relatively short periods of treatment.

  2. EFX resolved NASH and improved fibrosis by ≥1 stage among patients homozygous for the PNPLA3 allele who are at high risk of progression to cirrhosis.

• Evidence of fibrosis improvement without correlation to LIC normalization corresponds to EFX’s potential to have direct anti-fibrotic effects.

• Insulin resistance appears to be an important prerequisite for NASH resolution in patients with poorer overall metabolic health.

• Akero’s Phase II studies, HARMONY (F2-F3) and SYMMETRY (F4), evaluating improvement in fibrosis after EFX treatment for 24 and 36 weeks, respectively, will determine if longer treatment durations increase response rates by categorical definitions of NASH resolution and fibrosis improvement.

• The extent of regression of fibrosis did not appear to be dependent on magnitude of liver fat reduction or extent of resolution of steatohepatitis.

• Suggests EFX has a direct and fibrotic effect independent of improvement in LFC and overall metabolic health.

• Larger duration of treatment with EFX may be required to see ≥1 stage improvement in fibrosis in the group with qualitative features of fibrosis regression, but no scarring change.

• There were no obvious pretreatment traits, or difference in responsiveness to EFX among the study population in regards to signs of fibrosis regression after 16 weeks of EFX treatment.

REFERENCES


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DISCLOSURES

EFX is indicated for treatment of patients with biopsy-confirmed NASH. Healthcare professionals are encouraged to review the prescribing information and consult with their local customer service representative for further details.

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