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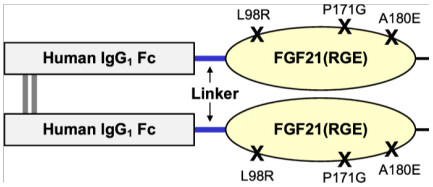


Efruxifermin

Developer(s)

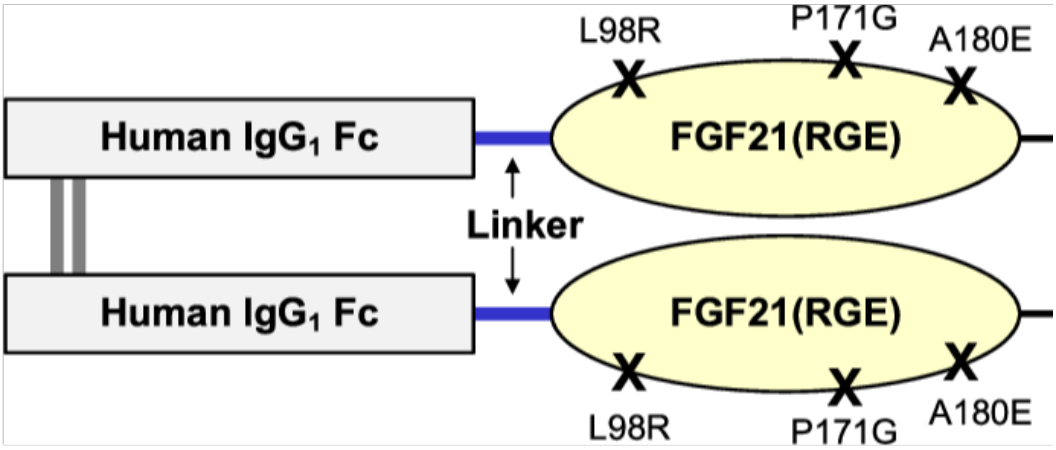
Akero Therapeutics

Originator

https://akerotx.com/

United States

Drug structure



Efruxifermin

Punegel et al. 2023

Drug information

Associated long-acting platforms

Monoclonal antibodies and antibody drug conjugates

Administration route

Subcutaneous

Therapeutic area(s)

Other(s) : "MASH"

Use case(s)

Treatment

Use of drug

Ease of administration

Administered by a nurse
Administered by a specialty health worker
Self-administered

User acceptance

Not provided

Dosage

Available dose and strength

Not provided

Frequency of administration

Not provided

Maximum dose

Not provided

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB19012

Generic name

Efruxifermin (EFX)

Brand name

investigational

Compound type

Biotherapeutic

Summary

EFX has been engineered to mimic the biological activity of fibroblast growth factor 21 (FGF21), which regulates multiple metabolic pathways and cellular processes. By delivering sustained and balanced signalling through FGF21’s receptors in liver and adipose tissue, EFX has the potential to treat MASH by addressing all core drivers of disease progression. EFX leverages the whole body to improve metabolic balance. The first Phase 2b study evaluated the efficacy and safety of EFX in patients with pre-cirrhotic MASH, fibrosis stage 2 or 3 (F2-F3). The study met its primary endpoint of ≥1 stage improvement in fibrosis with no worsening of MASH after 24 weeks of treatment for both the 50 mg EFX (41%) and 28 mg EFX (39%) dose groups, compared to 20% for the placebo arm.

Approval status

Unknown

Regulatory authorities

Unknown

Delivery device(s)

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Not provided

Clinical trials

AK-US-001-0106

Identifier

NCT06528314

Link

https://clinicaltrials.gov/study/NCT06528314

Phase

Phase III

Status

Recruiting

Sponsor

Akero Therapeutics, Inc

More details

This is a multi-center evaluation of efruxifermin (EFX) in a randomized, double-blind, placebo-controlled study in subjects with compensated cirrhosis due to NASH/MASH.

Purpose

A Study Evaluating Efruxifermin in Subjects With Compensated Cirrhosis Due to NASH/MASH

Interventions

Intervention 1

Efruxifermin

Dosage: 50 mg subcutaneous

Intervention 2

Placebo

Dosage: subcutaneous

Countries

United States of America

Australia

Argentina

Canada

Chile

France

Germany

India

Israel

Italy

Korea, Republic of

Puerto Rico

Spain

Switzerland

Türkiye

United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2024-09-04

Anticipated Date of Last Follow-up

2025-05-23

Estimated Primary Completion Date

2029-09-01

Estimated Completion Date

2029-10-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All
- Male
- Female

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Cohort 1: Biopsy proven compensated cirrhosis (fibrosis stage 4) due to NASH/MASH * Cohort 2: Biopsy proven or non-invasively diagnosed compensated cirrhosis (fibrosis stage 4) due to NASH/MASH Exclusion Criteria: * Other causes of liver disease based on medical history and/or liver histology and/or central laboratory results * Type 1 diabetes or unstable Type 2 diabetes * Any current or prior history of decompensated liver disease Other inclusion and exclusion criteria may apply

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

1150

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Primary outcome: Time from randomization to first occurrence of disease progression as measured by composite of protocol-specified clinical events (5 years)

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Once

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Not provided

AK-US-001-0105

Identifier

NCT06215716

Link

https://clinicaltrials.gov/study/NCT06215716

Phase

Phase III

Status

Recruiting

Sponsor

Akero Therapeutics, Inc

More details

This is a multi-center evaluation of efruxifermin (EFX) in a randomized, double-blind, placebo-controlled study in subjects with non-cirrhotic NASH/MASH and fibrosis stage 2 or 3 (F2 or F3). The study will enroll subjects in two cohorts for a total samples size of 1650 subjects.

Purpose

A Study Evaluating Efruxifermin in Subjects With Non-Cirrhotic Nonalcoholic Steatohepatitis (NASH)/Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Fibrosis

Interventions

Intervention 1

Efruxifermin

Dosage: 28 mg subcutaneous injection

Intervention 2

Efruxifermin

Dosage: 50 mg subcutaneous injection

Intervention 3

Placebo

Dosage: subcutaneous injection

Countries

United States of America

Argentina

Australia

Canada

France

Germany

India

Israel

Italy

Korea, Republic of

Poland

Puerto Rico

Spain

Switzerland

Taiwan, Province of China

Türkiye

United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-12-01

Anticipated Date of Last Follow-up

2025-05-09

Estimated Primary Completion Date

2032-11-01

Estimated Completion Date

2032-11-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All
- Male
- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Males and non-pregnant, non-lactating females between 18 - 80 years of age inclusive, based on the date of the screening visit. * Previous history or presence of 2 out of 4 components of metabolic syndrome (obesity, dyslipidemia, elevated blood pressure, elevated fasting glucose) or type 2 diabetes. * Cohort 1: Biopsy-proven NASH/MASH. Must have had a liver biopsy obtained ≤ 180 days prior to screening with fibrosis stage 2 or 3 and a non-alcoholic fatty liver disease (NAFLD) activity score (NAS) of ≥ 4 with at least a score of 1 in each of the following NAS components: * Steatosis (scored 0 to 3), * Ballooning degeneration (scored 0 to 2), and * Lobular inflammation (scored 0 to 3). Exclusion Criteria: * Other causes of liver disease based on medical histor

Health status

Not provided
Other health status: Subjects With Non-Cirrhotic Nonalcoholic Steatohepatitis (NASH)/Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Fibrosis

Study type

Interventional (clinical trial)

Enrollment

1650

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Once

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Not provided

AK-US-001-0107

Identifier

NCT06161571

Link

https://clinicaltrials.gov/study/NCT06161571

Phase

Phase III

Status

Enrolling by invitation

Sponsor

Akero Therapeutics, Inc

More details

The aim of this study is to assess the safety and tolerability of EFX compared to placebo in subjects with non-invasively diagnosed NASH/MASH and NAFLD/MASLD.

Purpose

A Study Evaluating Efruxifermin in Subjects With Non-invasively Diagnosed Nonalcoholic Steatohepatitis (NASH)/Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Nonalcoholic Fatty Liver Disea

Interventions

Intervention 1

Efruxifermin

Dosage: 50 mg subcutaneous injection

Intervention 2

Efruxifermin (open label)

Dosage: 50 mg subcutaneous injection

Intervention 3

Placebo

Dosage: subcutaneous injection

Countries

United States of America

Argentina

Australia

Canada

India

Israel

Korea, Republic of

Mexico

Puerto Rico

Switzerland

Taiwan, Province of China

United Kingdom

Türkiye

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-11-10

Anticipated Date of Last Follow-up

2025-01-31

Estimated Primary Completion Date

2026-04-01

Estimated Completion Date

2026-10-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All
- Male
- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: Main Study Only: * Males and non-pregnant, non-lactating females between 18 - 80 (between 19-80 in the Republic of Korea) years of age inclusive, on the day of signing informed consent * Previous history or presence of 2 out of 4 components of metabolic syndrome (obesity, dyslipidemia, elevated blood pressure, elevated fasting glucose) or type 2 diabetes * Suspected or confirmed diagnosis of NASH/MASH or NAFLD/MASLD or non-invasively diagnosed NASH/MASH or NAFLD/MASLD Open-Label Rollover * Prior participation in the placebo arm of a previous Akero Phase 2 study Exclusion Criteria: * Other causes of liver disease based on medical history and/or liver histology and/or central laboratory results, including but not limited to: alcoholic liver disease, autoimmune disor

Health status

Not provided
Other health status: Subjects With NASH/MASH and NAFLD/MASLD

Study type

Interventional (clinical trial)

Enrollment

700

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Once

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Not provided

20100018

Identifier

NCT01856881

Link

https://clinicaltrials.gov/study/NCT01856881

Phase

Phase I

Status

Terminated

Sponsor

Amgen

More details

The purpose of this study is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics following ascending multiple doses of AMG 876 in subjects with type 2 diabetes.

Purpose

Multiple Ascending Dose Study in Subjects With Type 2 Diabetes

Interventions

Not provided

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2013-03-01

Anticipated Date of Last Follow-up

2015-11-05

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2014-11-01

Actual Completion Date

2015-03-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Male and female subjects ≥ 18 to ≤ 65 years of age at the time of randomization * Female subjects must be of documented non-reproductive potential * Diagnosed with type 2 diabetes * HbA1c ≥ 6.5% and ≤ 10% * Fasting C-peptide value ≥ 0.8 ng/mL * Body mass index (BMI) between ≥ 25.0 and ≤ 40.0 kg/m2 at screening Exclusion Criteria: * Female subjects who are lactating/breastfeeding or who plan to breastfeed while on study through 4 weeks after receiving the last dose of study drug. * Male subjects with partners who are pregnant or planning to become pregnant while the subject is on study through 4 weeks after receiving the last dose of study drug * Evidence or history at screening of diabetic complications with significant end-organ damage, eg, proliferative retinopat

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

86

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key resources

Not provided

20100015

Identifier

NCT01492465

Link

https://clinicaltrials.gov/study/NCT01492465

Phase

Phase I

Status

Terminated

Sponsor

Amgen

More details

The purpose of this study is to determine whether AMG 876 is safe and well tolerated in subjects with type 2 diabetes.

Purpose

Single Ascending Dose Trial in Patients With Type 2 Diabetes

Interventions

Not provided

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2011-11-01

Anticipated Date of Last Follow-up

2013-02-13

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2012-07-01

Actual Completion Date

2012-10-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Subject has provided written informed consent * Men and women between the ages of 18 and 65, inclusive at the time of randomization * Women must be of documented non-reproductive potential (ie, postmenopausal \[see definition below\]; OR history of hysterectomy; OR history of bilateral tubal ligation; OR history of bilateral oophorectomy). * Diagnosed with type 2 diabetes * HbA1c ≥ 6.5% and ≤ 10% * Fasting C-peptide value ≥ 0.8 ng/mL * Men must agree for the duration of the study and continuing for 4 weeks after the dose of study drug, to practice a highly effective method of birth control. Highly effective methods of birth control include sexual abstinence, vasectomy or a condom with spermicide (men) in combination with either barrier methods, hormonal birth control

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

47

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key resources

Not provided

Harmony

Identifier

NCT04767529

Link

https://clinicaltrials.gov/study/NCT04767529

Phase

Phase II

Status

Completed

Sponsor

Akero Therapeutics, Inc

More details

This is a multi-center evaluation of efruxifermin (EFX) in a randomized, double-blind, placebo-controlled study in non-cirrhotic subjects with biopsy-proven F2 - F3 NASH.

Purpose

A Study of Efruxifermin in Non-Cirrhotic Subjects With Histologically Confirmed Nonalcoholic Steatohepatitis (NASH)

Interventions

Not provided

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-02-16

Anticipated Date of Last Follow-up

2025-04-23

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-05-02

Actual Completion Date

2024-05-02

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Males and non-pregnant, non-lactating females between 18 - 75 years of age inclusive, based on the date of the screening visit. * Previous history or presence of 2 out of 4 components of metabolic syndrome (obesity, dyslipidemia, elevated blood pressure, elevated fasting glucose) or type 2 diabetes. * FibroScan measurement \> 8.5 kPa \[kilopascal\]. * Biopsy-proven NASH. Must have had a liver biopsy obtained ≤ 180 days prior to randomization with fibrosis stage 2 to 3 and a non-alcoholic fatty liver disease (NAFLD) activity score (NAS) of ≥ 4 with at least a score of 1 in each of the following NAS components: * Steatosis (scored 0 to 3), * Ballooning degeneration (scored 0 to 2), and * Lobular inflammation (scored 0 to 3). Exclusion Criteria: * Weight loss \

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

128

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key resources

Not provided

Excipients

Proprietary excipients used

Not provided

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

Not provided

Residual solvents used

Not provided

Patent info

Description

Efruxifermin compositions

Brief description

Efruxifermin compositions, comprising sugar, arginine/arginine-HCl or arginine/glutamic acid, and a surfactant disclosed in different ratios and concentrations

Representative patent

WO2023064808

Category

Formulation

Patent holder

AKERO THERAPEUTICS, INC.

Exclusivity

Not provided

Expiration date

September 11, 2043

Status

Pending: AE, AP, AU, BR, CA, CL, CN, CO, CR, EA, EG, EP, HK, ID, IL, IN, JO, JP, KR, MA, MX, MY, NZ, PA, PE, PH, SA, SG, TH, UA, US, VN, ZA

Description

Method of Treatment using Efruxifermin

Brief description

Method of treating metabolic disorder (incl. type 1 diabetes, obesity etc.) using Efruxifermin (SEQ ID NO 41)

Representative patent

WO2013033452

Category

Method of treatment

Patent holder

AMGEN INC.

Exclusivity

Not provided

Expiration date

August 30, 2032

Status

Granted: AU Pending: JP, MX, US Not in force: EP

Description

Specific Efruxifermin polypeptides

Brief description

Efruxifermin polypetide sequence specifically claimed as SEQ ID NO 47

Representative patent

WO2010129503

Category

Compound

Patent holder

AMGEN INC.

Exclusivity

Not provided

Expiration date

May 4, 2030

Status

Granted: AR, BR, AU, CA, CN, CO, CR, EA (KZ, RU), EP (CH, DE, FR, IT, GB, LI), HK, IN, ID, IL, JP, KR, LB, MY, MX, MA, NZ, PA, GC, PE, PH, SG, ZA, TH, TW, TN, UA, US Pending: BW, EG, JO, LY, VN

Description

Broad Efruxifermin polypeptides

Brief description

Broad FGF21 mutant polypeptides, covering mutants of Efruxifermin IgG constant domain as SEQ ID NO 13 and Efruxifermin FGF21 as SEQ ID NO 4, and tris(tetraglycylseryl) peptide linker as SEQ ID NO 23 Full Efruxifermin sequence not disclosed

Representative patent

WO2009149171

Category

Compound

Patent holder

AMGEN INC.

Exclusivity

Not provided

Expiration date

June 3, 2029

Status

Granted: DZ, AU, BR, CA, CN, CO, EA (KZ, RU), EP (CH, DE, FR, GB, LI), HK, IN, ID, IL, JP, KR, MY, MX, MA, NZ, PE, SG, ZA, TW, TN, UA, US, VN Pending: AR, BW, CL, CR, EG, JO, LY, GC, UY

Supporting material

Publications

Shanaka Stanislaus, Randy Hecht, Junming Yie, Todd Hager, Michael Hall, Chris Spahr, Wei Wang, Jennifer Weiszmann, Yang Li, Liying Deng, Dwight Winters, Stephen Smith, Lei Zhou, Yuesheng Li, Murielle M. Véniant, Jing Xu, A Novel Fc-FGF21 With Improved Resistance to Proteolysis, Increased Affinity Toward *β*-Klotho, and Enhanced Efficacy in Mice and Cynomolgus Monkeys, *Endocrinology*, Volume 158, Issue 5, 1 May 2017, Pages 1314–1327, https://doi.org/10.1210/en.2016-1917

Fibroblast growth factor (FGF) 21 is a natural hormone that modulates glucose, lipid, and energy metabolism. Previously, we engineered an Fc fusion FGF21 variant with two mutations, Fc-FGF21(RG), to extend the half-life and reduce aggregation and *in vivo* degradation of FGF21. We now describe a new variant developed to reduce the extreme C-terminal degradation and improve the binding affinity to *β*-Klotho. We demonstrate, by introducing one additional mutation located at the C terminus of FGF21 (A180E), that the new molecule, Fc-FGF21(RGE), has gained many improved attributes. Compared with Fc-FGF21(RG), Fc-FGF21(RGE) has similar *in vitro* potency, preserves *β*-Klotho dependency, and maintains FGF receptor selectivity and cross-species reactivity. *In vivo*, Fc-FGF21(RGE) showed reduced susceptibility to extreme C-terminal degradation and increased plasma levels of the bioactive intact molecule. The circulating half-life of intact Fc-FGF21(RGE) increased twofold compared with that of Fc-FGF21(RG) in mice and cynomolgus monkeys. Additionally, Fc-FGF21(RGE) exhibited threefold to fivefold enhanced binding affinity to coreceptor *β*-Klotho across mouse, cynomolgus monkey, and human species. In obese and diabetic mouse and cynomolgus monkey models, Fc-FGF21(RGE) demonstrated greater efficacies to Fc-FGF21(RG), resulting in larger and more sustained improvements in multiple metabolic parameters. No increased immunogenicity was observed with Fc-FGF21(RGE). The superior biophysical, pharmacokinetic, and pharmacodynamic properties, as well as the positive metabolic effects across species, suggest that further clinical development of Fc-FGF21(RGE) as a metabolic therapy for diabetic and/or obese patients may be warranted.

Puengel, T., & Tacke, F. (2023).Efruxifermin, an investigational treatment for fibrotic or cirrhotic nonalcoholic steatohepatitis (NASH). *Expert Opinion on Investigational Drugs*, *32*(6), 451–461. https://doi.org/10.1080/13543784.2023.2230115

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease and strongly associated with metabolic disorders: obesity, type 2 diabetes (T2D), cardiovascular disease. Persistent metabolic injury results in inflammatory processes leading to nonalcoholic steatohepatitis (NASH), liver fibrosis, and ultimately cirrhosis. To date, no pharmacologic agent is approved for the treatment of NASH. Fibroblast growth factor 21 (FGF21) agonism has been linked to beneficial metabolic effects ameliorating obesity, steatosis, and insulin resistance, supporting its potential as a therapeutic target in NAFLD.

Areas covered

Efruxifermin (EFX, also AKR-001 or AMG876) is an engineered Fc-FGF21 fusion protein with an optimized pharmacokinetic and pharmacodynamic profile, which is currently tested in several phase 2 clinical trials for the treatment of NASH, fibrosis and compensated liver cirrhosis. EFX improved metabolic disturbances including glycemic control, showed favorable safety and tolerability, and demonstrated antifibrotic efficacy according to FDA requirements for phase 3 trials.

Expert opinion

While some other FGF-21 agonists (e.g. pegbelfermin) are currently not further investigated, available evidence supports the development of EFX as a promising anti-NASH drug in fibrotic and cirrhotic populations. However, antifibrotic efficacy, long-term safety and benefits (i.e. cardiovascular risk, decompensation events, disease progression, liver transplantation, mortality) remain to be determined.

Harrison SA, Frias JP, Neff G, et al. Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, phase 2b trial. *Lancet Gastroenterol Hepatol*. 2023;8(12):1080-1093. doi:10.1016/S2468-1253(23)00272-8

Background: Fibroblast growth factor 21 (FGF21) regulates metabolism and protects cells against stress. Efruxifermin is a bivalent Fc-FGF21 analogue that replicates FGF21 agonism of fibroblast growth factor receptor 1c, 2c, or 3c. The aim of this phase 2b study was to assess its efficacy and safety in patients with non-alcoholic steatohepatitis (NASH) and moderate (F2) or severe (F3) fibrosis.

Methods: HARMONY is a multicentre, randomised, double-blind, placebo-controlled, 96-week, phase 2b trial that was initiated at 41 clinics in the USA. Adults with biopsy-confirmed NASH, defined by a non-alcoholic fatty liver disease activity score (NAS) of 4 or higher and scores of 1 or higher in each of steatosis, ballooning, and lobular inflammation, with histological stage F2 or F3 fibrosis, were randomly assigned (1:1:1), via an interactive response system, to receive placebo or efruxifermin (28 mg or 50 mg), subcutaneously once weekly. Patients, investigators, pathologists, site staff, and the sponsor were masked to group assignments during the study. The primary endpoint was the proportion of patients with improvement in fibrosis of at least 1 stage and no worsening of NASH, based on analyses of baseline and week 24 biopsies (liver

biopsy analysis set [LBAS]). A sensitivity analysis evaluated the endpoint in the full analysis set (FAS), for which patients with missing biopsies were considered non-responders. This trial is registered with ClinicalTrials.gov, NCT04767529, and is ongoing.

Findings: Between March 22, 2021, and Feb 7, 2022, 747 patients were assessed for eligibility and 128 patients (mean age 54·7 years [SD 10·4]; 79 [62%] female and 49 male [38%]; 118 [92%] white; and 56 [41%] Hispanic or Latino) were enrolled and randomly assigned to receive placebo (n=43), efruxifermin 28 mg (n=42; two randomised patients were not dosed because of an administrative error), or efruxifermin 50 mg (n=43). In the LBAS (n=113), eight (20%) of 41 patients in the placebo group had an improvement in fibrosis of at least 1 stage and no worsening of NASH by week 24 versus 15 (39%) of 38 patients in the efruxifermin 28 mg group (risk ratio [RR] 2·3 [95% CI 1·1-4·8]; p=0·025) and 14 (41%) of 34 patients in the efruxifermin 50 mg group (2·2 [1·0-5·0]; p=0·036). Based on the FAS (n=128), eight (19%) of 43 patients in the placebo group met this endpoint versus 15 (36%) of 42 in the efruxifermin 28 mg group (RR 2·2 [95% CI 1·0-4·8]; p=0·033) and 14 (33%) of 43 in the efruxifermin 50 mg group (1·9 [0·8-4·3]; p=0·123). The most frequent efruxifermin-related adverse events were diarrhoea (16 [40%] of 40 patients in the efruxifermin 28 mg group and 17 [40%] of 43 patients in efruxifermin 50 mg group vs eight [19%] of 43 patients in the placebo group; all events except one were grade 1-2) and nausea (11 [28%] patients in the efruxifermin 28 mg group and 18 [42%] patients in the efruxifermin 50 mg group vs ten [23%] patients in the placebo group; all grade 1-2). Five patients (two in the 28 mg group and three in the 50 mg group) discontinued due to adverse events. Serious adverse events occurred in four patients in the 50 mg group; one was defined as drug related (ulcerative esophagitis in a participant with a history of gastro-oesophageal reflux disease). No deaths occurred.

Interpretation: Efruxifermin improved liver fibrosis and resolved NASH over 24 weeks in patients with F2 or F3 fibrosis, with acceptable tolerability, supporting further assessment in phase 3 trials.

Additional documents

No documents were uploaded

Useful links

- Efruxifermin summary by Akero

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided