A Placebo-controlled study of Maralixibat in Subjects with Progressive Familial Intrahepatic Cholestasis (MARCH-PFIC)

11/08/2025 11:31:26

Main Information

Primary registry identifying number
LBCTR2020063422

Protocol number
MRX-502

MOH registration number

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
05/04/2019

Primary sponsor
Mirum Pharmaceuticals Inc

Primary sponsor: Country of origin
California

Date of registration in primary registry
18/06/2020

Date of registration in national regulatory agency
05/04/2019

Public title
A Placebo-controlled study of Maralixibat in Subjects with Progressive Familial Intrahepatic Cholestasis (MARCH-PFIC)

Acronym
N/A

Scientific title
MRX-502: Randomized Double-blind Placebo-controlled Phase 3 Study to Evaluate the Efficacy and Safety of Maralixibat in the Treatment of Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC) – MARCH-PFIC

Acronym
N/A

Brief summary of the study: English

This is a 6-month, international, multicenter, randomized, double-blind, placebo-controlled Phase 3 study in subjects with PFIC. The study will be followed by the long-term extension study MRX-503, during which all subjects who complete study MRX-502 will have the opportunity to be treated with maralixibat. The purpose of this study is to determine if the investigational treatment (maralixibat) is safe and effective in pediatric participants with Progressive Familial Intrahepatic Cholestasis (PFIC).

Brief summary of the study: Arabic

دراسة لمده سته اشهر مرحلة ثالثة عشوائية مزدوجة التعمية محكومة بدواء وهمي لتقييم أمان ماراليكسيبات وفعاليته في علاج المرضى موضوع الهدف منها تحديد اذا كان الدواء ماراليكسابات امن و فعال ((PFIC)الدراسة المصابين بمرض الركود الصفراوي العائلي التقدمي داخل الكبد على المرضى الاطفال ام لا.

Health conditions/problem studied: Specify

Evaluate the Efficacy and Safety of Maralixibat in the Treatment of Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC)

Interventions: Specify

Drug: Maralixibat
Maralixibat oral solution (up to 600 mcg/kg) orally twice daily for 26 weeks.
Other Name: Formerly LUM001 and SHP625

Other: Placebo
Placebo matching to maralixibat orally twice daily for 26 weeks.

Key inclusion and exclusion criteria: Inclusion criteria

Informed consent and assent (as applicable) per Institutional Review Board/Ethics Committee (IRB/EC)
2. Male or female subjects with a body weight ≥ 5 kg, who are ≥12 months and < 18 years of age at time of consent
3. Cholestasis as manifested by total sBA ≥ 3× ULN
4. An average AM ItchRO(Obs) score ≥ 1.5 during 4 consecutive weeks of the screening period, leading to the baseline visit (Visit 1)
5. Completion of at least 21 valid* morning ItchRO(Obs) entries during 4 consecutive weeks of the screening period, leading to the baseline visit (Visit 1) (*valid = completed and not answered as "I don't know"; maximum allowed invalid reports = 7, no more than 2 invalid reports during the last 7 days before randomization)
6. Diagnosis of PFIC based on the following:
Chronic cholestasis as manifested by persistent (>6 months) pruritus, biochemical abnormalities or pathological evidence of progressive liver disease
and
Primary Cohort:
Subjects with genetic testing results consistent with biallelic disease-causing variation in ABCB11 (PFIC2), based on standard of care genotyping
Supplemental Cohort:
i. Subjects with genetic testing results consistent with biallelic disease-causing variation in ATP8B1 (PFIC1), ABCB4 (PFIC3), or TJP2 (PFIC4), based on standard of care genotyping
ii. Subjects with PFIC phenotype without a known mutation or with another known mutation not described above
iii. Subjects with PFIC after internal or external biliary diversion surgery or for whom internal or external biliary diversion surgery was reversed
7. Male and females of non-childbearing potential. Males and non-pregnant, non-lactating females of childbearing potential who are sexually active must agree to use acceptable contraception during the study and 30 days following the last dose of the study medication. Females of childbearing potential must have a negative pregnancy test
8. Access to email or phone for scheduled remote visits
9. Ability to read and understand the questionnaires (both caregivers and subjects above the age of assent)
10. Access to consistent caregiver(s) during the study
11. Subject and caregiver willingness to comply with all study visits and requirements

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

1

Key inclusion and exclusion criteria: Age maximum

17

Key inclusion and exclusion criteria: Exclusion criteria

Predicted complete absence of bile salt excretion pump (BSEP) function based on the type of ABCB11 mutation (PFIC2), as determined by a standard of care genotyping (applies to primary cohort only).
History of surgical disruption of the enterohepatic circulation (applies to primary cohort only)
3. Chronic diarrhea requiring intravenous fluid or nutritional intervention for the diarrhea and/or its sequelae at screening or during the 6 months prior to screening
4. Previous or planned liver transplant
5. Decompensated cirrhosis (international normalized ratio [INR] > 1.5, albumin < 30 g/L, history or presence of clinically significant ascites, variceal hemorrhage, and/or encephalopathy)
6. ALT or total serum bilirubin (TSB) > 15× ULN at screening
7. Presence of other liver disease
8. Presence of any other disease or condition known to interfere with the absorption, distribution, metabolism or excretion of drugs, including bile salt metabolism in the intestine (e.g., inflammatory bowel disease), per Investigator discretion
9. Liver mass on imaging, including screening ultrasound
10. Known diagnosis of human immunodeficiency virus (HIV) infection
11. Any prior cancer diagnosis (except for in situ carcinoma) within 5 years of the screening visit (Visit 0)
12. Any known history of alcohol or substance abuse
13. Administration of bile acids or lipid binding resins, or sodium phenylbutyrate during the screening period
14. Administration of growth hormones at any time before or during the study
15. Administration of any investigational drug, biologic, or medical device during the screening period
16. Previous use of an ileal bile acid transporter inhibitor (IBATi)

17. History of non-adherence to medical regimens, unreliability, medical condition, mental instability or cognitive impairment that, in the opinion of the Investigator or Sponsor medical monitor, could compromise the validity of informed consent, compromise the safety of the subject, or lead to nonadherence with the study protocol or inability to conduct the study procedures
18. Known hypersensitivity to maralixibat or any of its excipients

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

Dose escalation

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP	Year of authorization	Month of authorization
Maralixibat	2019	4

Type of IMP

Others

Pharmaceutical class

Maralixibat is an inhibitor of the apical sodium-dependent bile acid transporter/ileal bile acid transporter/solute carrier family 10 (sodium/bile acid cotransporter family) member 2 (ASBT/IBAT/SLC10A2), a transmembrane protein localized on the luminal surface of ileal enterocytes.

Therapeutic indication

Evaluate the Efficacy and Safety of Maralixibat in the Treatment of Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC).

Therapeutic benefit

Maralixibat was designed to be minimally absorbed, therefore maximizing the local exposure of the molecule to the receptor and minimizing systemic exposure of the drug and limiting drug-drug interactions and systemic toxicity. These characteristics include a high molecular weight of 740 Da, and the addition of a positively charged quaternary amino moiety that can interact with the negatively charged surface of the enterocyte cell membrane and prevent absorption. Also The pharmacokinetics (PK), safety, and efficacy of maralixibat were assessed in a previous clinical development program that evaluated maralixibat as a potential lipid-lowering agent in patients with hypercholesterolemia.
The efficacy and long term safety of maralixibat in the treatment of cholestatic liver disease in pediatric subjects with PFIC) indicate that a subgroup of subjects with PFIC2 experienced clinically significant improvements on maralixibat treatment as manifested by a large reduction or normalization of sBA, reduction in pruritus (ItchRO[Obs]), and normalization of elevated bilirubin, alanine and aspartate aminotransferase (ALT andAST) for those subjects with elevated baseline values.

Study model

N/A

Study model: Explain model

Study model: Specify model
N/A

N/A

Time perspective
N/A

Time perspective: Explain time perspective
N/A

Time perspective: Specify perspective
N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention
Samples without DNA

Biospecimen description
Blood Samples

Target sample size
30

Actual enrollment target size
3

Date of first enrollment: Type
Actual

Date of first enrollment: Date
09/07/2019

Date of study closure: Type
Actual

Date of study closure: Date
31/12/2020

Recruitment status
Recruiting

Recruitment status: Specify

Date of completion

IPD sharing statement plan
Yes

IPD sharing statement description
The Sponsor and/or its representatives accessing the records and data will take all reasonable precautions in accordance with applicable laws, regulations, and guidelines to maintain the confidentiality of subjects' identities. Subjects are assigned a unique identifying number; however, their initials and date of birth may also be collected, if permitted under local laws governing privacy

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
US NCT	NCT03905330

Sources of Monetary or Material Support

Name
Mirum Pharmaceuticals Inc. 950 Tower LaneFoster City, CA 94404

Secondary Sponsors

Name
N/A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Chadi Safa	Beirut	Lebanon	009617125 1819	chadi.safa@clinart.net	Clinart
Scientific	Adib Moukarzel	HDF	Lebanon	009613516 060	adib.moukarzel@usj.edu.lb	Hotel Dieu De France

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Adib Moukarzel	Gastroenterology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	01/10/2019	Nancy Choucair Alam	nancy.alam@usj.edu.lb	961 1 421 000 ext 2335

Countries of Recruitment

Name
Lebanon
Argentina
Austria
Belgium
Brazil
Canada
Colombia
France
Germany
Hungary
Italy
Mexico
Poland
Singapore
Turkey
United Kingdom
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
Progressive Familial Intrahepatic Cholestasis	Pruritus (L29)	PFIC

Interventions

Intervention	Description	Keyword
Maralixibat Chloride	Inhibitor of the apical sodium-dependent bile acid transporter/ileal bile acid transporter/solute carrier family 10 (sodium/bile acid cotransporter family) member 2 (ASBT/IBAT/SLC10A2)	Maralixibat
Placebo	Placebo contain only the following excipient :lactose monohydrate, microcrystalline methylcellulose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate.	Placebo

Primary Outcomes

Name	Time Points	Measure
To evaluate the efficacy of maralixibat vs placebo on the severity of pruritus in the primary cohort	Normalisation of sBA	PIS, CIS and IchRO

Key Secondary Outcomes

Name	Time Points	Measure
To evaluate the efficacy of maralixibat vs. placebo on the frequency of pruritus in the primary cohort	Stop of Pruritis	PIS,CIS and ICHro
To evaluate the efficacy of maralixibat vs. placebo on total serum bile acid (sBA) levels in the primary cohort	Normalisation of sBA	sBA

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files