



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

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## 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 لمدة ستة اشهر مرحلة ثالثة عشوائية مزدوجة التعمية محكمة بدواء وهمي لتقييم امان ماراليكسابات وفعاليتها 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  $\geq 5$  kg, who are  $\geq 12$  months and  $< 18$  years of age at time of consent
3. Cholestasis as manifested by total sBA  $\geq 3 \times$  ULN
4. An average AM ItchRO(Obs) score  $\geq 1.5$  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)  $> 15 \times$  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**

Maralixibat

**Year of authorization**

2019

**Month of authorization**

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 Lane Foster 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	0096171251819	chadi.safa@clinart.net	Clinart
Scientific	Adib Moukarzel	HDF	Lebanon	009613516060	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**