Evaluate the Pharmacokinetics and Safety of Etavopivat in Pediatric Patients with Sickle Cell Disease

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Main Information

Primary registry identifying number
LBCTR2022095118

Protocol number
4202-HEM-202

MOH registration number

Study registered at the country of origin
No

Study registered at the country of origin: Specify
Poor pool of patients with Sickle Cell Disease

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
26/09/2022

Primary sponsor
Forma Therapeutics, Inc.

Primary sponsor: Country of origin
United States of America

Date of registration in primary registry
25/10/2022

Date of registration in national regulatory agency
26/09/2022

Public title
Evaluate the Pharmacokinetics and Safety of Etavopivat in Pediatric Patients with Sickle Cell Disease

Acronym

Scientific title
A Single Arm, Open Label, Phase 1/2 Study to Evaluate the Pharmacokinetics and Safety of Etavopivat in Pediatric Patients with Sickle Cell Disease

Acronym

Brief summary of the study: English
This clinical trial is a Phase 1/2 study that will evaluate the Pharmacokinetics and Safety of Etavopivat (FT-4202) in Pediatric Patients from 12 to 18 years with Sickle Cell Disease to improve the amount of hemoglobin in the blood and to reduce the number of vaso-occlusive crises (times when the blood vessels become blocked and cause pain).

Brief summary of the study: Arabic
هذه التجربة السريرية هي دراسة المرحلة 1/2 التي ستقيم الحرائك الدوائية وسلامة Etavopivat (FT-4202) في مرضى الأطفال الذين تتراوح أعمارهم بين 12 و 18 عامًا المصابين بمرض الخلايا المنجلية لتحسين كمية الهيموجلوبين في الدم وتقليل العدد من أزمات انسداد الأوعية الدموية (الأوقات التي يتم فيها انسداد الأوعية الدموية وتسبب الألم).

Health conditions/problem studied: Specify
Sickle Cell Disease

Interventions: Specify
Drug: Etavopivat (FT-4202)

Key inclusion and exclusion criteria: Inclusion criteria
Type of Participant and Disease Characteristics
1. Patient has confirmed diagnosis of SCD

• Documentation of SCD genotype (HbSS, HbSβ0-thalassemia or other sickle cell syndrome variants) based on prior history of laboratory testing. Molecular genotyping is not required. SCD genotype may be determined from the results of Hb electrophoresis, high-performance liquid chromatography (HPLC), or similar testing. Note that Hb electrophoresis is performed by the local laboratory at Screening.
2. Hemoglobin ≥ 5.5 and < 10.5 g/dL
3. Adolescent patients with severe SCD, as defined by at least 1 of the following:
• Two or more VOCs in the past 12 months, defined as a previously documented episode of acute chest syndrome (ACS) or acute painful crisis (for which there was no explanation other than VOC) which required prescription or healthcare professional-instructed use of analgesics for moderate to severe pain
• Hospitalization for any SCD-related complication in the last 12 months
• Proteinuria, defined as an albumin:creatinine ratio (ACR) > 100 mg/g on 2 measures (separated by ≥ 1 month) as an indicator of early renal disease
• History of a conditional TCD in the last 12 months, but not currently being treated with chronic transfusion therapy. Conditional TCD is defined as a TAMMV of 170-199 cm/s by TCD or 155-184 cm/s by imaging TCD (TCDi).
4. For participants taking HU, the dose of HU (mg/kg) must be stable (no more than a 20% change in dosing) for at least 90 days prior to start of study treatment with no anticipated need for dose adjustments during the study, in the opinion of the Investigator
5. Patients on crizanlizumab or L-glutamine treatment at the time of consent may be eligible if they:
• Have been on a stable dose for ≥ 12 months at the time of consent (ie, no changes to the dose except for changes to weight or for safety reasons)
• For patients on crizanlizumab, have been ≥ 80% compliant

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

12

Key inclusion and exclusion criteria: Age maximum

18

Key inclusion and exclusion criteria: Exclusion criteria

Medical Conditions
1. More than 10 VOCs within the past 12 months that required a hospital, emergency room (ER), or clinic visit
2. Hospitalized for sickle cell crisis or other vaso-occlusive event within 14 days of Screening
3. Abnormal TCD in the prior 12 months
Prior/Concomitant Therapy
4. Patients receiving regularly scheduled blood (RBC) transfusion therapy (also termed chronic, prophylactic, or preventive transfusion)
5. Received any blood products within 30 days of starting study treatment
6. Receiving or use of concomitant medications that are strong inducers of cytochrome P450 (CYP) 3A4/5 within 2 weeks of starting study treatment
7. Use of voxelotor within 28 days prior to starting study treatment or anticipated need for this agent during the study
8. Receipt of erythropoietin or other hematopoietic growth factor treatment within 28 days of starting study treatment or anticipated need for such agents during the study
9. Receipt of prior cellular based therapy (eg, hematopoietic cell transplant, gene modification therapy)

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Other

Trial scope: Specify scope

Study design: Allocation

Single Arm Study

Study design: Masking

Open (masking not used)

Study design: Control

Active

Study phase

1 to 2

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Single

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

-

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

Antianaemics- Pyruvate kinase red blood cell isozyme (PKR) agonist

Therapeutic indication

Sickle Cell Disease

Therapeutic benefit

Etavopivat is an investigational, oral, small molecule activator of erythrocyte pyruvate kinase (PKR) in development for the treatment of sickle cell disease (SCD) and other hemoglobinopathies. PKR activation is proposed to ameliorate the sickling of SCD red blood cells (RBCs) through multiple mechanisms, including reduction of 2,3-diphosphoglycerate (2,3-DPG), which consequently increases hemoglobin (Hb)-oxygen affinity; increased binding of oxygen reduces sickle hemoglobin polymerization and sickling. In addition, PKR activation increases adenosine triphosphate (ATP) produced via glycolytic flux, which helps preserve membrane integrity and RBC deformability.

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

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

PK and PD samples

Target sample size

8

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

15/11/2022

Date of study closure: Type

Date of study closure: Date

Anticipated

12/09/2026

Recruitment status

Pending

Recruitment status: Specify

Date of completion

IPD sharing statement plan

No

IPD sharing statement description

N/A

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
N/A	N/A

Sources of Monetary or Material Support

Name
Forma Therapeutics, Inc. USA

Secondary Sponsors

Name
N/A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Mohamed Salloum	Saint Therese street, Beirut	Lebanon	+961 81967 578	mohamed.salloum@iqvia.com	IQVIA
Scientific	Cameron Trenor	300 North Beacon Street, Suite 501 Watertown, MA 02472	United States of America	+1-857-209-2374	4202-202Clinical@formarx.com	Forma Therapeutics, Inc.

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Nini Hospital s.a.l.	Dr. Adlette Inati	Hematology	Approved
American University of Beirut Medical Center	Dr. Miguel Abboud	Hematology	Pending

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Nini Hospital	26/08/2022	Dr. Elias Bitar	-	+9616431400

Countries of Recruitment

Name
Lebanon
Canada

Health Conditions or Problems Studied

Condition	Code	Keyword
Sickle Cell	Sickle-cell disorders (D57)	Hematology, Blood diseases, Sickle Cell

Interventions

Intervention	Description	Keyword
Drug	Etavopivat (FT-4202)	-

Primary Outcomes

Name	Time Points	Measure
To assess the PK of etavopivat in patients with SCD	-	Single-dose: maximum concentration (Cmax), area under the concentration time curve (AUC)0-t, AUC0-inf
To assess the PK of etavopivat in patients with SCD	-	Steady-state etavopivat plasma exposure (Cmax,ss, AUCtau,ss, Cavg,ss, Cmin,ss)
To assess the PK of etavopivat in patients with SCD	-	Estimated using population PK
To assess the safety and tolerability of etavopivat	During the 24-week primary treatment period	Incidence of adverse events (AEs), serious adverse events (SAEs), and AEs related to etavopivat
To assess the safety and tolerability of etavopivat	During the 24-week primary treatment period	Number of premature discontinuations, dose interruptions, and dose reductions

Key Secondary Outcomes

Name	Time Points	Measure
To assess the safety and tolerability of etavopivat	during the 72-week treatment extension period	Incidence of AEs, SAEs, and AEs related to etavopivat
To assess the safety and tolerability of etavopivat	during the 72-week treatment extension period	Number of premature discontinuations, dose interruptions, and dose reductions
To assess the effects of etavopivat on hemoglobin (Hb) response	Weeks 12 and 24	Hb response rate (increase of > 1 g/dL from baseline)
To assess the effects of etavopivat on hemoglobin (Hb) response	Weeks 12 and 24	Change in Hb from baseline
To describe occurrence of vaso-occlusive crisis (VOCs) in enrolled patients	-	Change from baseline in incidence of VOCs during the treatment period of: Number of VOCs + Annualized Rate of VOC
To assess changes in fatigue of patients with SCD taking etavopivat	Weeks 12 and 24	Change from baseline in Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Scale
To assess changes in cerebral blood flow in patients with SCD taking etavopivat	-	Change from baseline in time-averaged mean of the maximum velocity (TAMMV) by transcranial Doppler ultrasonography (TCD)

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