



Study to Evaluate the Effect of GBT440 in Pediatrics With Sick Cell Disease

13/08/2025 11:01:23

Main Information

Primary registry identifying number

LBCTR2019090195

Protocol number

GBT440-007

MOH registration number

1288/ص

Study registered at the country of origin

Yes

Study registered at the country of origin: Specify

Type of registration

Retrospective

Type of registration: Justify

Requested by Sponsor- Registry not in place upon study initiation

Date of registration in national regulatory agency

11/06/2014

Primary sponsor

Global Blood Therapeutics Inc.

Primary sponsor: Country of origin

United States of America

Date of registration in primary registry

26/06/2024

Date of registration in national regulatory agency

11/06/2014

Public title

Study to Evaluate the Effect of GBT440 in Pediatrics With Sick Cell Disease

Acronym

Scientific title

A Phase 2a, Open-label, Single and Multiple Dose Study to Evaluate the Pharmacokinetics, Safety, Tolerability, and Exploratory Treatment Effect of GBT440 in Pediatric Participants With Sick Cell Disease

Acronym

Brief summary of the study: English

This study consists of three parts, Parts A, B, C and D.
- Part A is a single dose PK study in pediatric participants with Sick Cell Disease. (Closed on 07 Aug 2017 (LPLV))
- Part B is a multiple dose, safety, exploratory, efficacy, and PK study in adolescent Sick Cell Disease participants who were 12-17 years of age (Closed on 04 Jan 2019 (LPLV))
- Part C is a multiple dose, safety, tolerability, and PK study, which includes the assessment of hematological effects and the effect on TCD flow velocity of GBT440 in pediatric participants with Sick Cell Disease who are 4 to 17 years of age.
- Part D is a multiple dose study that will assess the safety, tolerability, and PK, as well as the hematological effects, of voxelotor in pediatric participants with SCD 6 months to < 4 years of age.

Brief summary of the study: Arabic

عند الأطفال المصابين بمرض الخلايا المنجلية GBT440 دراسة لتقييم تأثير

Health conditions/problem studied: Specify

Sick Cell Disease



Interventions: Specify

Drug: GBT440 administered as oral capsules, tablets, dispersible tablets or powder for oral suspension.

Key inclusion and exclusion criteria: Inclusion criteria

1. Male or female participants with homozygous hemoglobin SS (HbSS) or hemoglobin S beta0 thalassemia (HbS β 0 thal).
2. Age:
 - Part A – 6 to 17 years of age (Cohort 1 [12 to 17] and Cohort 2 [6 to 11] as defined in the Study Design)
 - Part B – 12 to 17 years of age
 - Part C – 4 to 17 years of age
 - Part D – 6 months to < 4 years of age
3. Hydroxyurea (HU) therapy:
 - Parts A, B, and C – A participant taking HU may be enrolled if the dose has been stable for at least 3 months with no anticipated need for dose adjustments during the study and no sign of hematological toxicity.
 - Part D – A participant taking HU may be enrolled if the dose has been stable for at least 1 month. Titration to the maximum tolerated dose (MTD) is allowed during the study.
4. Hemoglobin (Hb):
 - Part A – No restriction
 - Part B – Hb \leq 10.5 g/dL
 - Part C – Hb \leq 10.5 g/dL
 - Part D – Hb \leq 10.5 g/dL
5. Written informed parental/guardian consent and participant assent has been obtained per institutional review board (IRB)/Ethics Committee (EC) policy and requirements, consistent with ICH guidelines.
6. Participants in Part B (only) of the study must complete a minimum of 14 days with ePRO to be enrolled. Investigator discretion will be used to determine if a participant who has previously been screen failed due to a lack of baseline ePRO data collection can be invited back for rescreening.
7. If sexually active and female, must agree to abstain from sexual intercourse or to use a highly effective method of contraception throughout the study period and for 30 days after discontinuation of study drug. If sexually active and male, must agree to abstain from sexual intercourse or willing to use barrier methods of contraception throughout the study period and for 30 days after discontinuation of study drug.
8. Females of child-bearing potential are required to have a negative pregnancy test before the administration of study drug.
9. Sufficient venous access to permit collection of PK samples and monitoring of laboratory safety variables, in the opinion of the Investigator.
10. For Part C only, participants 12 to 17 years of age must have a TCD velocity \geq 140 cm/sec by nonimaging TCD or \geq 125 cm/sec by TCDi measured anytime during screening.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

0

Key inclusion and exclusion criteria: Age maximum

17

Key inclusion and exclusion criteria: Exclusion criteria

1. Any one of the following requiring medical attention within 14 days prior to signing the informed consent form (ICF):
 - Vaso-occlusive crisis (VOC)
 - Acute chest syndrome (ACS)
 - Splenic sequestration crisis
 - Dactylitis
 2. Requires chronic transfusion therapy.
 3. History of stroke or meeting criteria for primary stroke prophylaxis (history of two TCD measurements \geq 200 cm/sec by nonimaging TCD or \geq 185 cm/sec by TCDi).
 - For the potential modification, addition of approximately 20 participants enrolled in Part C, TCD \geq 170 cm/sec by nonimaging TCD or \geq 155 cm/sec by TCDi.
 4. Transfusion within 30 days prior to signing the ICF.
 5. Renal dysfunction requiring chronic dialysis or creatinine \geq 1.5 mg/dL.
 6. Hepatic dysfunction characterized by alanine aminotransferase (ALT) $>$ 4 \times upper limit of normal (ULN) for age.
 7. Clinically relevant cardiac abnormality, in the opinion of the Investigator, such as:
 - Hemodynamically significant heart disease, eg, congenital heart defect, uncompensated heart failure, or any unstable cardiac condition
 - An arrhythmic heart condition requiring medical therapy
 8. QTcF $>$ 450 msec, congenital long QT syndrome, second or third degree heart block at rest (with the exception of asymptomatic Mobitz type I second degree heart block).
 9. Received an investigational drug within 30 days or 5 half-lives, whichever is longer, of signing the ICF.
 10. Heavy smoker (defined as smoking more than 10 cigarettes/day or its nicotine equivalent including e-cigarettes).
 11. Unlikely to comply with the study procedures.
 12. Other medical, psychological, or addictive condition that, in the opinion of the Investigator, would confound or interfere with evaluation of safety and/or PK of the investigational drug, prevent compliance with the study protocol, or preclude informed consent.
 13. Participants who do not have a TCD window (Part B and C only) (ie, participants who are unable to have a TCD due to skull ossification).
 14. For Part C only, prior participation in Part B.
 15. Active symptomatic COVID-19 infection.
- In addition, for Part D only:
16. Body weight $<$ 5 kg for 1 month prior to the screening visit and at the screening visit.
 17. Any condition affecting drug absorption, such as major surgery involving the stomach or small intestine (prior cholecystectomy is acceptable).



18. History of malignancy within the past 2 years prior to treatment Day 1 requiring chemotherapy and/or radiation (with the exception of local therapy for non-melanoma skin malignancy).
19. Clinically significant bacterial, fungal, parasitic, or viral infection currently receiving or that will require therapy.
- Participants with acute bacterial infection requiring antibiotic use should delay screening until the course of antibiotic therapy has been completed and the infection has resolved, in the opinion of the investigator.
 - Known active hepatitis A, B, or C infection or human immunodeficiency virus (HIV)-positive.
 - Known active malaria.

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

N/A: Single arm study

Study design: Masking

Open (masking not used)

Study design: Control

Dose comparison

Study phase

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

Yes, Worldwide

IMP has market authorization: Specify

USA, UAE, EU, GB, Oman and Kuwait

Name of IMP

OXBRYTA

Year of authorization

2019

Month of authorization

11

Type of IMP

Others

Pharmaceutical class

Allosteric modulator of hemoglobin-oxygen affinity

Therapeutic indication

Sickle Cell Disease

Therapeutic benefit

Voxelotor is an orally bioavailable HbS polymerization inhibitor that binds specifically to HbS with a 1:1 stoichiometry, and exhibits preferential partitioning to RBCs. By increasing Hb's affinity for oxygen, voxelotor inhibits HbS polymerization in a dose dependent manner that may improve deformability, decrease the viscosity of SCD blood, and ultimately increase blood flow in the microcirculation, thus improving net O2 delivery. Therefore, chronically modifying 20% to 30% of HbS with voxelotor in subjects with SCD is expected to deliver the clinical benefits of reducing HbS polymerization while improving O2 delivery to peripheral tissues.

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**

None retained

Biospecimen description

N/A

Target sample size

24

Actual enrollment target size

38

Date of first enrollment: Type

Actual

Date of first enrollment: Date

21/07/2016

Date of study closure: Type

Actual

Date of study closure: Date

12/06/2024

Recruitment status

Complete

Recruitment status: Specify**Date of completion**

31/12/2023

IPD sharing statement plan

No

IPD sharing statement description

N/A

Additional data URL

<https://clinicaltrials.gov/ct2/show/NCT02850406>

Admin comments**Trial status**

Approved



Secondary Identifying Numbers

| Full name of issuing authority | Secondary identifying number |
|--------------------------------|------------------------------|
| Clinicaltrials.gov | NCT02850406 |
| EU Clinical Trials Registry | EudraCT: 2016-004209-15 |

Sources of Monetary or Material Support

| Name |
|-------------------------------------|
| Global Blood Therapeutics, Inc. USA |

Secondary Sponsors

No Sponsors

Contact for Public/Scientific Queries

| Contact type | Contact full name | Address | Country | Telephone | Email | Affiliation |
|--------------|-------------------|---|-----------------------------|----------------|--------------------------|--|
| Public | Dr. Adlette Inati | Tripoli | Lebanon | 9613228033 | adlette.inati@lau.edu.lb | Nini Hospital |
| Scientific | Mark Davis | 181 Oyster Point Blvd., South San Francisco, CA 94080 | United States of America | (925) 336-1055 | mdavis@gbt.com | Global Blood Therapeutics |
| Public | Dr. Miguel Abboud | Beirut | Lebanon | 9611350000 | ma56@aub.edu.lb | American University of Beirut Medical Center |

Centers/Hospitals Involved in the Study

| Center/Hospital name | Name of principles investigator | Principles investigator speciality | Ethical approval |
|--|---------------------------------|------------------------------------|------------------|
| American University of Beirut Medical Center | Dr. Miguel Abboud | Pediatric Hematology-Oncology | Approved |
| Rafik Hariri University Hospital | Dr. Adlette Inati | Pediatric Hematology-Oncology | Approved |
| Nini Hospital | Dr. Adlette Inati | Pediatric Hematology-Oncology | Approved |



Ethics Review

| Ethics approval obtained | Approval date | Contact name | Contact email | Contact phone |
|--|---------------|-------------------|----------------|---------------|
| American University of Beirut Medical Center | 09/07/2018 | Dr. Fuad Ziyadeh | irb@aub.edu.lb | 9611738025 |
| Rafic Hariri University Hospital | 31/08/2018 | Dr. Iyad Issa | NA | 9611830000 |
| Nini Hospital | 31/08/2018 | Dr. Nabil Kabbara | NA | 9616431400 |

Countries of Recruitment

| Name |
|--------------------------|
| Lebanon |
| United States of America |
| United Kingdom |

Health Conditions or Problems Studied

| Condition | Code | Keyword |
|---------------------|-----------------------------|--|
| Sickle Cell Disease | Sickle-cell disorders (D57) | Sickle Cell, Anemia, Hemolytic, Congenital, Hematologic Diseases |

Interventions

| Intervention | Description | Keyword |
|--------------|-------------|--|
| Drug | GBT440 | Oral Capsule, Tablet, Dispersible Tablet or Powder for Oral Suspension |



Primary Outcomes

| Name | Time Points | Measure |
|---|-----------------------|-----------------------------|
| Part A: Pharmacokinetic profile of GBT440 including maximum concentration | Pre-dose to Day 15 | Pharmacokinetic profile |
| Part A: Pharmacokinetic profile of GBT440 including the time taken to reach the maximum concentration | Pre-dose to Day 15 | Pharmacokinetic profile |
| Part A: Pharmacokinetic profile of GBT440 including the total drug concentration over time | Pre-dose to Day 15 | Pharmacokinetic profile |
| Part B: Change in hemoglobin | Baseline to Week 24 | Hemoglobin in Blood |
| Part C: Change in cerebral blood flow | Baseline to Week 48 | TAMM TCD velocity |
| Part D | During Study Duration | Incidence of TEAEs and SAEs |

Key Secondary Outcomes

| Name | Time Points | Measure |
|---|---------------------------------|--|
| Part A: Number of participants with treatment-related adverse events | Days 1 - 15 | Assessed by CTCAE v4.03 |
| Part B: Multiple Dose effect on Clinical Measures of Hemolysis | Day 1 - Week 24 | Clinical Measures of Hemolysis |
| Part B: Pharmacokinetic profile of GBT440 including maximum concentration | Pre-dose to Week 24 | Pharmacokinetic profile |
| Part B: Pharmacokinetic profile of GBT440 including the time taken to reach the maximum concentration | Pre-dose to Week 24 | Pharmacokinetic profile |
| Part B: Pharmacokinetic profile of GBT440 including the total drug concentration over time | Pre-dose to Week 24 | Pharmacokinetic profile |
| Part C: Multiple dose effect on clinical measures of hemolysis | Baseline to Week 24 and Week 48 | Clinical Measures of Hemolysis |
| Part C: Change in cerebral blood flow | Baseline to Week 24 | Measured by the TAMM TCD velocity |
| Part C: Pharmacokinetic profile of GBT440 including maximum concentration | Pre-Dose to Week 48 | Pharmacokinetic profile |
| Part C: Pharmacokinetic profile of GBT440 including the time taken to reach the maximum concentration | Pre-Dose to Week 48 | Pharmacokinetic profile |
| Part C: Pharmacokinetic profile of GBT440 including the total drug concentration over time | Pre-Dose to Week 48 | Pharmacokinetic profile |
| Part D: Whole blood and plasma voxelotor PK (Cmax, AUC, t1/2, if appropriate) and occupancy | Baseline to Week 24 and Week 48 | Change in Hb, LDH, indirect bilirubin, and reticulocyte count |
| Part D: Whole blood and plasma voxelotor PK (Cmax, AUC, t1/2, if appropriate) and occupancy | - | Time to initial Hb response, defined as change from baseline in Hb > 1g/dL |
| Part D: Whole blood and plasma voxelotor PK (Cmax, AUC, t1/2, if appropriate) and occupancy | During whole study duration | Incidence of stroke and VOC |



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