An Open-label Extension Study to Evaluate the Long-term Safety of Inclacumab Administered to Participants with Sickle Cell Disease Who Have Participated in an Inclacumab Clinical Trial

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Main Information

Primary registry identifying number
LBCTR2021074838

Protocol number
GBT2104-133

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
05/07/2021

Primary sponsor
Global Blood Therapeutics, Inc.

Primary sponsor: Country of origin
USA

Date of registration in primary registry
18/02/2022

Date of registration in national regulatory agency
05/07/2021

Public title
An Open-label Extension Study to Evaluate the Long-term Safety of Inclacumab Administered to Participants with Sickle Cell Disease Who Have Participated in an Inclacumab Clinical Trial

Acronym

Scientific title
An Open-label Extension Study to Evaluate the Long-term Safety of Inclacumab Administered to Participants with Sickle Cell Disease Who Have Participated in an Inclacumab Clinical Trial

Acronym

Brief summary of the study: English
This multicenter, global, open-label extension study is designed to assess the safety of long-term treatment with inclacumab in participants with sickle cell disease (SCD). The study will be conducted globally and will be available to eligible participants enrolled in a prior sponsored inclacumab clinical study. Participants must have completed participation in their originating clinical study and must meet the entry criteria for this study to be eligible for enrollment.

The primary objective of this study is to evaluate the long-term safety of every 12-week dosing of inclacumab in participants with SCD who have completed a prior inclacumab clinical trial.

Brief summary of the study: Arabic

تم تصميم هذه الدراسة الموسعة متعددة المراكز والعالمية والمفتوحة التسمية لتقييم سلامة العلاج طويل الأمد باستخدام inclacumab للمشاركين المصابين بمرض الخلايا المنجلية. سيتم إجراء الدراسة على مستوى العالم وستكون متاحة للمشاركين المؤهلين المسجلين في دراسة إكلينيكية سابقة لنفس الراعي. يجب أن يكون المشاركون قد أكملوا المشاركة في دراستهم السريرية الأصلية ويجب أن يستوفوا inclacumab معايير الدخول لهذه الدراسة ليكونوا مؤهلين للتسجيل.

الغرض الرئيسي من هذه الدراسة هو تقييم سالمة وتأثير الجرعات المزمنة طويلة الألمد من إنكالكوماب لدى المشاركين الذين شاركوا في دراسة سابقة على عقار إنكالكوماب.

Health conditions/problem studied: Specify

Up to approximately 520 participants who have completed a prior inclacumab clinical trial will be enrolled.

Interventions: Specify

This multicenter, global, open-label extension study is designed to assess the safety of long-term treatment with inclacumab in participants with SCD. The study will be conducted globally and will be available to eligible participants enrolled in a prior Global Blood Therapeutics, Inc. (GBT)-Sponsored inclacumab clinical study (originating study). Participants must have completed participation in their originating clinical study and must meet the entry criteria for this study to be eligible for enrollment. The study will be conducted at up to 150 global clinical sites, and up to approximately 520 participants will be enrolled.
Eligible participants will receive inclacumab 30 mg/kg administered intravenously (IV) Q12W if they continue to receive clinical benefit that outweighs risk, as determined by the Investigator, until the participant has access to inclacumab from an alternative source (eg, through commercialization or a managed-access program).
All participants will undergo safety and outcome assessments at Baseline (Day 1), Week 6, and every 12 weeks thereafter. Visits to the clinical site for infusion of study drug will occur at Baseline (Day 1) and every 12 weeks (Weeks 12, 24, 36, 48, etc.).

Key inclusion and exclusion criteria: Inclusion criteria

Participants who meet all the following criteria will be eligible for study enrollment:

1. Male or female participant with SCD who participated and received study drug in a GBT-Sponsored inclacumab clinical study.
2. Participant has completed the originating inclacumab study within 30 calendar days of the Day 1 Visit. Participants who discontinued study drug in the originating study due to a non-study drug-related adverse event (AE), but who remained on study, may be eligible for treatment in this study provided the AE does not pose a risk for treatment with inclacumab.
3. Female participants of childbearing potential are required to have a negative urine pregnancy test prior to dosing on Day 1.
Note: Female participants who become of childbearing potential during the study must be willing to have a negative urine pregnancy test to remain in the study.
4. If sexually active, female participants of childbearing potential must consistently use highly effective methods of contraception consistently throughout the study and for at least 165 days after the last dose of study drug. If sexually active, male participants must use barrier methods of contraception until 165 days after the last dose of study drug.
5. Participant has provided written informed consent/assent. For underage participants, both the consent of the participant's legal representative or legal guardian and the participant's assent (where applicable) must be obtained based on local requirement.

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

90

Key inclusion and exclusion criteria: Exclusion criteria

Participants meeting any of the following exclusion criteria will not be eligible for study enrollment:
1. Female participant who is breastfeeding or pregnant.
2. Participant had an infusion-related reaction (IRR) in the originating inclacumab clinical study.
3. Participant withdrew consent from the originating inclacumab clinical study.
4. Participant was lost to follow-up from the originating inclacumab clinical study.
5. Participant has any medical, psychological, safety, or behavioral conditions that, in the opinion of the Investigator, may confound safety interpretation, interfere with compliance, or preclude informed consent.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Safety

Trial scope: Specify scope

N/A

Study design: Allocation

Single Arm Study

Study design: Masking

Open (masking not used)

Study design: Control

N/A

Study phase

3

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

Inclacumab

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

Inclacumab is a recombinant human monoclonal antibody (huMAb) of the immunoglobulin (Ig)G4 subclass directed against human P-selectin, which is being developed by GBT, for the treatment of SCD. Inclacumab binds to P-selectin, which is a cell adhesion molecule produced by endothelial cells and platelets. Upon activation of these cells (e.g., by thrombin, cytokines, complement components, hypoxia, and heme), P-selectin is translocated to the cell surface where it binds to its primary ligand P-selectin glycoprotein ligand-1 (PSGL-1) and mediates leukocytes recruitment by platelets or endothelial cells. The same mechanism is also responsible for abnormal rolling and adhesion of sickle red blood cells (RBC) to the endothelium, initiating acute vascular occlusion and chronically impairing microvascular blood flow in patients with SCD. Inclacumab binding of P-selectin and prevention of P-selectin binding to its ligands is the putative mechanism by which inclacumab prevents the binding of sickle RBCs or leukocytes to endothelium.

Therapeutic indication

sickle cell disease (SCD)

Therapeutic benefit

Inclacumab is a recombinant huMAb of the IgG4 subclass directed against human P-selectin. The molecule is composed of two heterodimers, each composed of a heavy and a light polypeptide chain. The four polypeptide chains are linked together by disulfide bonds. To avoid antibody-dependent cell-mediated cytotoxicity and to improve structural stability, two single point mutations (L235E, S228P) were introduced into the Fc part of the molecule. The inclacumab drug substance is manufactured by fermentation cell culture using Chinese hamster ovary (CHO) cells followed by purification. The drug substance, drug product, and placebo are manufactured in accordance with Good Manufacturing Practices (GMP). Results from the SUSTAIN trial in patients with SCD showed that treatment with crizanlizumab, a humanized antibody to P-selectin, resulted in a significantly lower rate of sickle cell-related pain crises (i.e., vaso-occlusive crisis (VOC)) than placebo. These data validated P-selectin as a therapeutic
target for SCD disease. Inclacumab is currently not approved by any health authority for the treatment of patients with any disease. Inclacumab is being developed to reduce the risk of vaso-occlusive crises in patients with SCD.

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

Time perspective: Specify perspective

N/A

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

520

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

01/10/2021

Date of study closure: Type

Anticipated

Date of study closure: Date

31/12/2028

Recruitment status

Pending

Recruitment status: Specify

Date of completion

31/12/2028

IPD sharing statement plan

Yes

IPD sharing statement description

Patient's full identity will not be on any of the study documents or sample collected and kept by the sponsor for their studies. Only the partial date of birth will be only collected. Only a unique participant number for the study will link the data or samples to the patients.

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
Global Blood Therapeutics, Inc.

Secondary Sponsors

Name
N.A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Aziz Zoghbi	MCT-CRO, Berytech Technology and Health, 5th Floor Damascus Road, Beirut, Lebanon	Lebanon	009613534213	aziz.zoghbi@mct-cro.com	Director of Country Oversight and Management MENA, Gulf and Africa
Scientific	Miguel Abboud	American University of Beirut Medical Center, Cairo Street, Hamra, Beirut, Lebanon	Lebanon	009613534213	ma56@aub.edu.lb	PI
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Scientific	Carolyn Hoppe	181 Oyster Point Blvd. South San Francisco, CA 94080, USA	United States of America	+1 650 822 8728	choppe@gbt.com	Medical Monitor

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Nini Hospital	Adlette Inati	Professor of Pediatric Hematology and Oncology	Approved
American University of Beirut Medical Center	Miguel Abboud	Professor of Pediatric Hematology and Oncology	Pending

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Nini Hospital	23/06/2021	Nabil Kabbara	nabil.kabbara@hopitalnini.com	+961 (0) 6 431 400 ext 1062

Countries of Recruitment

No Countries

Health Conditions or Problems Studied

Condition	Code	Keyword
Sickle Cell Disease	Sickle-cell disorders (D57)	SCD

Interventions

Intervention	Description	Keyword
Inclacumab	All participants will receive inclacumab 30 mg/kg administered IV Q12W. All infusions of inclacumab will be administered at the study site.	Treatment

Primary Outcomes

Name	Time Points	Measure
Safety	each visit	Incidence of treatment-emergent adverse events (TEAEs).
Safety	each visit	Change from Baseline in laboratory assessments (hematology, chemistry, and coagulation).
Safety	each visit	Vital signs and physical examination

Key Secondary Outcomes

No Outcomes

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