A Phase 2 Study of PTG-300 in Non-Transfusion Dependent (NTD) and Transfusion-Dependent (TD) β-Thalassemia Subjects with Chronic Anemia

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Main Information

Primary registry identifying number
LBCTR2019020179

Protocol number
PTG300-02

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
01/02/2019

Primary sponsor
Protagonist Therapeutics Inc

Primary sponsor: Country of origin
USA

Date of registration in primary registry
23/03/2022

Date of registration in national regulatory agency
01/02/2019

Public title
A Phase 2 Study of PTG-300 in Non-Transfusion Dependent (NTD) and Transfusion-Dependent (TD) β-Thalassemia Subjects with Chronic Anemia

Acronym

Scientific title
A Phase 2 Study of PTG-300 in Non-Transfusion Dependent (NTD) and Transfusion-Dependent (TD) β-Thalassemia Subjects with Chronic Anemia

Acronym

Brief summary of the study: English

This is a Phase 2 open-label, single-arm study with dose escalation by subject cohort and with the potential for individual titration (dose increase or decrease) within each cohort. The primary objectives of the study is to evaluate the safety and tolerability of PTG-300 in subjects with Non-Transfusion Dependent (NTD) and Transfusion Dependent (TD) β-thalassemia. To obtain preliminary evidence of to obtain preliminary evidence of PTG-300's efficacy for treating chronic anemia in subjects with β-thalassemia and to identify the optimal starting dose, titration algorithm, dose range and dose regimen to be used in Phase 3 studies.

Brief summary of the study: Arabic

دراسة مرحلة2 أهداف الرئيسية، وذراع واحد مع تصعيد الجرعة حسب الفئات الموضوع وإمكانية معايرة الفردية داخل كل فئة. فتح التسمية
لهذه الدراسة تقييم السلامة وقابليةالتحمل
لعلاج PTG-300 المصابون بمرض بيتا ثلاسيميا المعتمد على نقل الدم و غير المعتمد على نقل الدم.

Health conditions/problem studied: Specify

Chronic anemia due to ineffective erythropoiesis (IE) in subjects with β thalassemia

Interventions: Specify

Five PTG-300 dose levels/regimens are planned to be tested for each subpopulation of β thalassemia (NTD and TD) on separate arms:
•Cohort 1: 3mg subcutaneous (SC) weekly (n = 6 subjects per subpopulation)
•Cohort 2: 10mg SC weekly (n = 6 subjects per subpopulation)
•Cohort 3: 20mg SC weekly (n = 6 subjects per subpopulation)
•Cohort 4a: 40mg SC weekly (n = 6 subjects per subpopulation)
•Cohort 4b: 40mg SC every 2 weeks (n = 6 subjects per subpopulation)
Two additional cohorts (Cohorts 5 and 6, n=6/cohort per subpopulation) will include subjects between 12-<18 years of age at a starting dose of 3mg and 10mg/weekly respectively, with the potential for individual titration (dose increase or decrease) based on the titration algorithm

Key inclusion and exclusion criteria: Inclusion criteria

All subjects must meet ALL of the following inclusion criteria to be enrolled:
1.Male and female subjects aged 18 to 65 years, inclusive (Cohorts 1 4b).
2.Male and female subjects aged 12-<18 years, with a minimum weight of 30 kg (Cohorts 5 and 6).
3.Documented diagnosis of β-thalassemia with no other Hgb abnormality.
4.Women of childbearing potential (WOCBP) and men agree to use a highly effective contraceptive measure (based on the Clinical Trial Facilitation Group [CTFG]) during the duration of the study and for 28 days after the last dose of study drug in the case of women and 90 days after the last dose of study drug in the case of men, as described in Appendix 1.
5.For WOCBP, a negative serum pregnancy test at screening and a negative urine pregnancy test within 24 hours prior to the first dose of study medication.
6.Subjects or legal guardians (in the case of minors) understand the study procedures and agree to participate in the study by giving written informed consent.
7.Subjects, or legal representative (in the case of minors), are willing and able to adhere to the study visit schedule and other protocol requirements.
8.Subjects between 12-<18 years of age understand and provide the assent to participate in the study, according to local guidelines.
Inclusion criteria applicable only for NTD β-thalassemia subjects:
1.Mean Hgb < 10.0 g/dL of two measurements (one performed 7–28 days prior to dosing and the other performed within 7 days prior to dosing).
2.Requirement of < 6 units RBC transfusion in a 24 week period with the last transfusion at least 8 weeks before screening.
Inclusion criteria applicable only for TD β-thalassemia subjects:
1.Transfusion requirement of at least 6 units of RBC in the 24 weeks prior to randomization with no transfusion free period > 45 days.
2.Last RBC transfusion 5–10 days prior to dosing.

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

65

Key inclusion and exclusion criteria: Exclusion criteria

Subjects must meet NONE of the following exclusion criteria to be enrolled:
1.Subjects with the diagnosis of β-thalassemia major (genotype homozygous β0/β0 or compound heterozygous β0/β+ with a major phenotype).
2.Infection requiring hospitalization or IV antimicrobial therapy, or opportunistic infection within 6 months of dosing, any infection requiring antimicrobial therapy within 2 weeks of dosing; history of infection with human immunodeficiency virus (HIV).
3.Subject has a concurrent clinically significant, unstable or uncontrolled cardiovascular, pulmonary, hepatic, renal, gastrointestinal, genitourinary, hematological, coagulation, immunological, endocrine/metabolic or other medical disorder that, in the opinion of the Investigator, might confound the results of the study or pose additional risk to the subject by their participation in the study.
4.Known primary or secondary immunodeficiency.
5.History within 6 months of screening of any of the following: myocardial infarction, unstable angina, transient ischemic attack, decompensated heart failure requiring hospitalization, congestive heart failure (New York Heart Association Class 3 or 4), uncontrolled arrhythmias, cardiac revascularization, stroke, uncontrolled hypertension (resting systolic blood pressure [BP] > 160mmHg or resting diastolic BP > 100mmHg on more than one occasion) or uncontrolled diabetes (Hgb A1c > 9% or > one episode of severe hypoglycemia).
6.Clinically meaningful laboratory abnormalities at screening including, but not limited to, the ranges below:
a.Absolute neutrophil count < 1000/µL
b.Platelet count < 100,000/µL
c.Estimated glomerular filtration rate (eGFR) < 60
d.Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥ 2.5 x upper limit of normal (ULN) or direct bilirubin > 1.5 x ULN
7.Treatment with hydroxyurea ≤ 24 weeks prior to randomization.
8.Use of erythropoiesis-stimulating agent (ESA) ≤ 24 weeks prior to randomization.
9.Chronic use of systemic glucocorticoids (anti-inflammatory dose for more than 14 days) ≤ 12 weeks prior to randomization (physiologic replacement therapy for adrenal insufficiency is allowed).
10.Pregnant or lactating females.
11.Any surgical procedure requiring general anesthesia within 1 month prior to screening or planned elective surgery during the study.
12.History of malignant neoplasms within 5 years prior to screening. Subjects who are cancer-free for the 5 years before screening may be enrolled. Subjects with carcinoma in situ, adequately treated non-metastatic basal cell skin cancer, or squamous cell skin cancer that has not recurred for at least 1 year prior to screening, may be enrolled.
13.Current or recent history of alcohol dependence or illicit drug use within 1 year prior to screening.
14.Subject is mentally or legally incapacitated at the time of screening visit or has a history of clinically significant psychiatric disorders that would impact the subject's ability to participate in the trial according to the Investigator. Note: Subjects who have had situational depression or adjustment disorder or treated depression may be enrolled at the discretion of the Investigator.
15.Concurrent participation in any other interventional study.

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

No

IMP has market authorization: Specify

Name of IMP

PTG-300

Year of authorization

Month of authorization

Type of IMP

Cell therapy

Pharmaceutical class

PTG-300 is a peptidic agent structurally related to natural hepcidin that mimics its inhibitory activity on ferroportin.

Therapeutic indication

β thalassemia

Therapeutic benefit

Administration of PTG-300 may result in iron redistribution in β-thalassemia subjects with potentially beneficial effects on erythropoiesis and consequently improvements in chronic anemia. This improvement in ineffective erythropoiesis may result in a clinical benefit both in NTD and in TD β-thalassemia subjects, by improving the symptomatology of the chronic anemia and the complications of the extramedullary hematopoiesis in the first group and by decreasing the need for transfusions in the latter.

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

Samples without DNA

Biospecimen description

Blood samples taken throughout the study will be shipped to ICON lab in Ireland for analysis. These samples will be then stored at ICON Lab by Protagonist Therapeutics for up to 10 years.

Target sample size

84

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

11/03/2019

Date of study closure: Type

Anticipated

Date of study closure: Date

21/07/2020

Recruitment status

Complete

Recruitment status: Specify

Date of completion

IPD sharing statement plan

Yes

IPD sharing statement description

Patients' full identity will not be on any of the study documents or samples collected and kept by the sponsor for their studies. The full or partial date of birth will only be collected if medically relevant to this study. Only a unique participant number for the study will link the data or samples to the patients. These data may contain your gender and race, as well as any medical and scientific data required by the study.

Additional data URL

none

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Food and Drug Administration	IND 137605

Sources of Monetary or Material Support

Name
Protagonist Therapeutics.inc

Secondary Sponsors

Name
Not applicable

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	009611612500	zog_az@mct-cro.com	Regional Manager
Scientific	Ali Taher	Chronic Care Center, Hazmieh, Lebanon	Lebanon	009613755669	ataher@aub.edu.lb	PI

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Chronic Care Center	Dr. Ali Taher	Professor of Medicine, Hematology & Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Chronic Care Center	02/12/2018	Michele Abi Saad	cccmas@chroniccare.org.lb	05-455101
American University of Beirut Medical Center	18/02/2019	Dr. Deborah Mukherji	irb@aub.edu.lb	01-350000 ext 5445

Countries of Recruitment

Name
Lebanon
Thailand
United Kingdom
United States of America
Turkey
Tunisia
Malaysia
Greece
Italy

Health Conditions or Problems Studied

Condition	Code	Keyword
Thalassemia	Thalassaemia (D56)	Thalassemia

Interventions

Intervention	Description	Keyword
PTG300	3mg subcutaneous (SC) weekly (n = 6 subjects per subpopulation)	Cohort 1
PTG300	10mg SC weekly (n = 6 subjects per subpopulation)	Cohort 2
PTG300	20mg SC weekly (n = 6 subjects per subpopulation)	Cohort 3
PTG300	40mg SC weekly (n = 6 subjects per subpopulation)	Cohort 4a
PTG300	40mg SC every 2 weeks (n = 6 subjects per subpopulation)	Cohort 4b

Primary Outcomes

Name	Time Points	Measure
NTD patients: Mean Hgb change from baseline	4-week period under the same dose	Hemoglobin test at each dose
NTD subjects who achieve an increase in Hgb ≥ 1.0 g/dL without transfusion	4-week period under the same dose.	Hemoglobin test at each dose
TD Patients: achieve ≥ 20% reduction in the RBC units required over an 8 week period	8 week period	RBC units transfused
TD patients: Mean change from baseline in the number of units of RBC required under each dose	8 week period	RBC units transfused

Key Secondary Outcomes

Name	Time Points	Measure
NTD patients: Mean Hgb	at the end of treatment	Hgb test
Proportion of subjects who achieve an increase in Hgb ≥ 1.5 g/dL	at any time up to Week 12 in NTD	Hgb test
Duration of response	NTD: Hgb change of ≥1 g/dL without transfusion; or ≥ 20% reduction in the RBC units required over an 8 week period in TD patients	Hbg test in NT; RBC units transfused in TD
Time to response	Hgb change of ≥1 g/dL without transfusion in NTD or ≥ 20% reduction in the RBC units required over an 8 week period in TD	Hbg test in NT; RBC units transfused in TD
TD patients: Mean number of RBC units required	at each dose over the 16 week period	RBC units transfused
Change from baseline in liver iron content	Week 16 for TD or week 12 for NTD	LIC measured by MRI

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