A Phase 2a, Randomized, Open-Label Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ISIS 702843 Administered Subcutaneously to Patients with Non-Transfusion Dependent β-Thalassemia Intermedia

14/11/2026 02:12:04

Main Information

Primary registry identifying number
LBCTR2020071296

Protocol number
ISIS 702843-CS2

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

Primary sponsor
Ionis Pharmaceuticals, Inc.

Primary sponsor: Country of origin
USA

Date of registration in primary registry
09/09/2020

Date of registration in national regulatory agency

Public title
A Phase 2a, Randomized, Open-Label Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ISIS 702843 Administered Subcutaneously to Patients with Non-Transfusion Dependent β-Thalassemia Intermedia

Acronym

Scientific title
A Phase 2a, Randomized, Open-Label Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ISIS 702843 Administered Subcutaneously to Patients with Non-Transfusion Dependent β-Thalassemia Intermedia

Acronym

Brief summary of the study: English
This is a Phase 2a, Randomized, Open-Label Study.The primary objective is to evaluate the Efficacy of antisense inhibitor of TMPRSS6 (ISIS 702843) by demonstrating an improvement in plasma hemoglobin (Hb) concentration at Week 27 of treatment,at Week 53 of treatment.The secondary objectives are to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ISIS 702843 Administered Subcutaneously to Patients with Non-Transfusion Dependent β-Thalassemia Intermedia

Brief summary of the study: Arabic

أ ، دراسة عشوائية مفتوحة التسمية. الهدف الرئيسي هو تقييم فعالية مثبط العقاقير من2هذه الدراسة في المرحلة TMPRSS6 (ISIS 702843) من خلال إظهار تحسن في تركيز الهيموغلوبين في البلازما (Hb) في الأسبوع 27من العلاج53 من العلاج ، في الأسبوع تحت الجلد ل ISIS 702843 الأهداف الثانوية هي تقييم السلامة ، التحمل ، الدوائية والديناميكا
الثلاسيميا إنترميديا-β المرضى الذين يعانون من عدم نقل الدم

Health conditions/problem studied: Specify

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

Interventions: Specify

The study will comprise 3 cohorts – Cohorts A, B, and C – of approximately 12 eligible patients per cohort:Cohort A (30 mg ISIS 702843), Cohort B (50 mg ISIS 702843), or Cohort C (80 mg ISIS 702843) in a ratio of 1:1:1.Each patient will be treated for up to 2 years, receiving up to 27 doses of
ISIS 702843, with a planned 28-day interval between each dose.

Key inclusion and exclusion criteria: Inclusion criteria

1. Patient must have given written informed consent and be able to comply with all study requirements
2. Aged 18-65 years old, inclusive, at the time of informed consent
3. Clinical diagnosis of β-Thalassemia Intermedia with genotypic confirmation of β-globin gene mutations including but not limited to Hemoglobin E
(HbE)/β-thalassemia
4. Patient must be non-transfusion dependent as defined by: No more than 6 transfusions in the past 12-month period, and no transfusions in the
8-week period prior to Day 1
5. Mean Hb within the range 6.0-10.0 g/dL, inclusive, with this mean based on all Hb measurements taken in the Screening Period that are at least
6 weeks after the most recent transfusion for that patient. This mean must be based on at least 2 Hb measurements
6. LIC within the range of 3.0-20.0 mg Fe/g dry weight, inclusive
7. Chelators will be permitted provided the patient has been on a stable dose for at least 3 months prior to Day 1, with LIC > 5.0 mg Fe/g dry weight
and serum ferritin > 300 ng/mL
8.Females must be non-pregnant and non-lactating, and one of the following: (i) surgically sterile (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy), (ii) postmenopausal (defined as 12 months of spontaneous amenorrhea without an alternative
medical cause and follicle stimulating hormone [FSH] levels in the postmenopausal range for the laboratory involved), (iii) abstinent, or (iv) if engaged in sexual relations of child-bearing potential, the patient must be using a highly effective contraceptive method from the time of signing the informed consent form until at least 13 weeks after the last dose of ISIS 702843 Males must be one of the following: (i) surgically
sterile, (ii) abstinent, or (iii) if engaged in sexual relations with a female of child-bearing potential, the patient must be using a highly effective contraceptive method from the time of signing the informed consent form until at least 13 weeks after the last dose of ISIS 702843.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

65

Key inclusion and exclusion criteria: Exclusion criteria

1. Genotypic confirmation of either α-globin gene triplication or sickle hemoglobin (HbS)/β-thalassemia, as determined by genetic assessment of
blood-related disorders
2. Clinically significant abnormalities in medical history or physical examination, which at the discretion of the PI will pose significant additional risk to
the patient in participating in the study
3. Clinically significant abnormalities in Screening laboratory values that would render a patient unsuitable for inclusion, at the discretion of the PI
4. Current use of iron-chelation therapy if LIC is 3.0–5.0 mg Fe/g dry weight, inclusive, or if serum ferritin ≤ 300 ng/mL
5. Symptomatic splenomegaly, including abdominal pain or organ obstruction, or evidence of hypersplenism, such as low white blood cell (WBC)
count and/or low platelets
6. Platelet count < LLN, or platelet count > 1,000 x 109/L
7. Significant concurrent/recent coagulopathy; history of non-traumatic significant bleeding; history of immune thrombocytopenic purpura (ITP); current use of SC anti-coagulants; history of thrombotic events, including stroke or deep vein thrombosis (DVT)
8. Clinically significant renal dysfunction which at the discretion of the PI will pose significant additional risk to the patient in participating in the study
9. Estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73 m2, using CKD-EPI
10. Clinically significant liver function test (LFT) abnormalities
11. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)> 3.0 × ULN
12. Historical diagnosis of cirrhosis, or current signs and symptoms of cirrhosis
13. Fasting blood glucose > 2.0 × ULN
14. Significant pulmonary hypertension (PHT) defined as tricuspid regurgitation > 3.0 meters per second (m/s) on echocardiography and/or

requiring
treatment
15. Uncontrolled hypertension (which for this protocol is considered > 140 mm Hg systolic or > 90 mm Hg diastolic)
16. Heart failure class 3 or higher (New York Heart Association, NYHA)
17. Ejection fraction < 50% by echocardiogram, multigated acquisition (MUGA), or cardiac magnetic resonance imaging (MRI)
18. Patients unable to have MRI performed, for example, because of a pacemaker or implantable cardioverter-defibrillator (MRI is being used to
measure LIC)
19. Active infection requiring systemic antiviral or antimicrobial therapy that will not be completed prior to Day 1
20. Known history of or positive test for human immunodeficiency virus (HIV), hepatitis C (unless treatment has caused the patient to test negative
for hepatitis C), or chronic hepatitis B
21. Unwillingness to comply with study procedures, including follow-up, as specified by this protocol, or unwillingness to cooperate fully with the Investigator
22. Recent introduction of hydroxyurea (within 6 months prior to Day 1)
23. Treatment with or exposure to another investigational drug, biological agent, ASO, small interfering ribonucleic acid (siRNA), or device within
one month of Screening, or 5 half-lives of investigational agent, whichever is longer; or:
-Treatment with or exposure to sotatercept (ACE-011), luspatercept (ACE-536), or ruxolitinib within 4 months of Screening
-Treatment with or exposure to hematopoietic stimulating agents (e.g., EPOs) or any hypoxia-inducible factor prolyl hydroxylase inhibitors
-Prior bone marrow transplant, stem cell transplant, or gene therapy
24. Regular use of alcohol within 6 months prior to Screening (> 7 drinks/wk for females, > 14 drinks/wk for males (1 drink = 5 ounces (150 mL) of
wine or 12 ounces (360 mL) of beer or 1.5 ounces (45 mL) of hard liquor)
25. Surgery associated with significant blood loss within 4 months of Screening, splenectomy within 12 months of Screening, or splenectomy scheduled during the Treatment Period
26. Use of iron supplements, including iron-containing vitamins, within 4 months of Screening
27. Pregnant or lactating
28. Have any other conditions which, in the opinion of the PI, would make the patient unsuitable for inclusion, or could interfere with the patient participating in or completing the 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

Randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

N/A

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

ISIS 702843

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

ISIS 702843 is an antisense inhibitor of transmembrane protease, serine 6 (TMPRSS6)

Therapeutic indication

Anemia and Iron overload in patients with Non-Transfusion Dependent β-Thalassemia Intermedia

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 for NTD β-thalassemia intermedia 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

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

blood sample will be taken for genotyping of B-globin variants and a genetic assessment of blood-related disorders that will include determination of α-globin copy number and whether the patient has exclusionary sickle hemoglobin (HbS)/B-thalassemia.
Blood and urine samples will be collected regularly throughout the study for efficacy, safety, PK, and PD analyses.

Target sample size

36

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

17/02/2020

Date of study closure: Type

Anticipated

Date of study closure: Date

31/12/2022

Recruitment status

Pending

Recruitment status: Specify

Date of completion

IPD sharing statement plan

Yes

IPD sharing statement description

Medical records of study subjects are stored and treated as confidential. The study site will record basic personal details including name, contact details, gender, height, weight, year of birth, age, ethnicity, and racial origin (to be used only for clinical purposes), as well as information on medical history, and clinical data collected about participation in the study. Medical records and other personal information will be treated as confidential.

Additional data URL

None

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Food and Drug Administration	EudraCT #: 2019-003505-96

Sources of Monetary or Material Support

Name
Ionis Pharmaceuticals, 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@mctcro.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	Hematology/Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	05/05/2020	Dr Deborah Mukherji	irb@aub.edu.lb	01-350000 ext 5445
Chronic Care Center	24/06/2020	Michele Abi Saad	cccmas@chroniccare.org.lb	05-455101

Countries of Recruitment

Name
Canada
Australia
Greece
Turkey
Thailand
Lebanon

Health Conditions or Problems Studied

Condition	Code	Keyword
Thalassemia	Thalassaemia (D56)	thalassemia

Interventions

Intervention	Description	Keyword
ISIS 702843	27 doses of 30 mg/0.3 mL	Cohort A
ISIS 702843	27 doses of 50 mg/0.5 mL	Cohort B
ISIS 702843	27 doses of 80 mg/0.8 mL	Cohort C

Primary Outcomes

Name	Time Points	Measure
HB ≥ 1.0 g/dL	Week 27 of treatment	Hemoglobin test

Key Secondary Outcomes

Name	Time Points	Measure
HB ≥ 1.5 g/dL increase from Baseline	Week 53 of treatment	Hemoglobin test
LIC ≥ 1.0 mg Fe/g dry weight decrease from Baseline	Week 53 of treatment	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