ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: IMR-BTL-201 A Study of IMR-687 in Subjects With Beta Thalassemia NCT04411082

Protocol Registration and Results Preview

This is a rough approximation of how the Protocol Registration and Results will appear on the ClinicalTrials.gov public web site.

A Study of IMR-687 in Subjects With Beta Thalassemia

ClinicalTrials.gov Identifier: NCT04411082

Recruitment Status: Terminated (IMR-BTL-201demonstrated that while IMR-687 was generally well-tolerated, it failed to show any meaningful benefit in transfusion burden or improvement in most disease-related biomarkers. So, the sponsor has decided to discontinue this study)
Results First Posted: *
First Posted: *
Last Update Posted: *

* Date not available in PRS

Sponsor:

Imara, Inc.

Information provided by (Responsible Party):

Imara, Inc.

Study Description

Brief Summary:

A Study to Evaluate the Safety and Tolerability of IMR-687 in Subjects with Beta Thalassemia

Condition or disease	Intervention/treatment	Phase
β Thalassemia	Drug: IMR-687 Drug: Placebo	Phase 2

Detailed Description:

A phase 2, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, PK, and PD of IMR-687 (phosphodiesterase (PDE) 9 inhibitor) administered once daily (qd) orally for 36 weeks in 2 populations of adult subjects with β-thalassemia: Population 1 (Transfusion Dependent Thalassemia (TDT) subjects) and Population 2 (Non-Transfusion Dependent Thalassemia (NTDT) subjects).

Study Design

Study Type: Interventional
Actual Enrollment: 122 participants
Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: None (Open Label)

Double-Blind

Primary Purpose: Treatment
Official Title: A Phase 2 Study to Evaluate the Safety and Tolerability of IMR-687 in Subjects With Beta Thalassemia

Actual Study Start Date: October 16, 2020
Actual Primary Completion Date: March 11, 2022
Actual Study Completion Date: May 4, 2022

Arms and Interventions

Arm	Intervention/treatment
Experimental: Lower Dose IMR-687 Oral administration of once daily IMR-687	Drug: IMR-687 Oral administration of once daily IMR-687
Experimental: Higher dose IMR-687 Oral administration of once daily IMR-687	Drug: IMR-687 Oral administration of once daily IMR-687
Placebo Comparator: Placebo Oral administration of once daily placebo	Drug: Placebo Oral administration of once daily Placebo

Outcome Measures

Primary Outcome Measure:

1. IMR-687 Safety and Tolerability [Time Frame: Baseline to Week 40]

   Incidence and severity of Adverse Events Incidence and severity of Serious Adverse Events

Secondary Outcome Measures:

1. TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥33% Hematological Improvement From Week 12 to Week 24 [Time Frame: Baseline to Week 24]

   Proportion of patients with ≥33% hematological improvement (as measured by reduced transfusion burden) from Week 12 to Week 24 compared to the 12 weeks prior to Baseline (Day 1)

2. NTDT Patients: Proportion of Subjects With an Increase From Baseline of Hb at Week 12 to Week 24 in the Absence of Transfusions. [Time Frame: Baseline to Week 24]

   Proportion of subjects with an increase from baseline of ≥1.0 g/dL in mean Hb values at Week 12 to Week 24 in the absence of transfusions.

3. NTDT Patients: Proportion of Subjects With an Increase From Baseline of ≥3% in Mean HbF Values at Week 12 to Week 24 in Absence of Transfusions [Time Frame: Baseline to Week 24]

   Proportion of subjects with an increase from baseline of ≥3% in mean HbF values at Week 12 to Week 24 in absence of transfusions

4. TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥33% Hematological Improvement From Week 24 to Week 36 [Time Frame: Baseline to Week 36]

   Proportion of patients with ≥33% hematological improvement from Week 24 to Week 36 compared to the 12 weeks prior to Baseline (Day 1)

5. TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥50 % Hematological Improvement From Week 12 to Week 24 [Time Frame: Baseline to Week 24]

   Proportion of patients with ≥50% hematological improvement from Week 12 to Week 24 compared to the 12 weeks prior to Baseline (Day 1)

6. TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥50% Hematological Improvement From Week 24 to Week 36 [Time Frame: Baseline to Week 36]

   Proportion of patients with ≥50% hematological improvement from Week 24 to Week 36 compared to the 12 weeks prior to Baseline (Day 1)

7. NTDT Patients: Proportion of Subjects With an Increase From Baseline of Hb at Week 24 to Week 36 in the Absence of Transfusions [Time Frame: Baseline to Week 36]

   Proportion of subjects with an increase from baseline of ≥1.0 g/dL in mean Hb values at Week 24 to Week 36 in the absence of transfusions.

8. NTDT: Proportion of Subjects With an Increase From Baseline of ≥3% in Mean HbF Values at Week 24 to Week 36 in Absence of Transfusions [Time Frame: Baseline to Week 36]

   Proportion of subjects with an increase from baseline of ≥3% in mean HbF values at Week 24 to Week 36 in absence of transfusions

Eligibility Criteria

Ages Eligible for Study:	18 Years to 65 Years
Sexes Eligible for Study:	All
Gender Based:	No
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Documented diagnosis of β-thalassemia or HbE/ β-thalassemia in their medical history. Concomitant alpha gene deletion, duplication, or triplication is allowed.
2. Documentation of the dates of transfusion events and the number of all pRBC units per event within the 12 weeks prior to the Baseline (Day 1) visit. .
3. Must be willing and able to complete all study assessments and procedures, and to communicate effectively with the investigator and site staff.
4. TDT Subjects: subjects must be regularly transfused, defined as >3 to 10 pRBC units in the12 weeks prior to Baseline (Day 1) visit and no transfusion-free period for >35 days during that period.
5. NTDT subjects: Subjects must be transfusion independent, defined as 0 to ≤3 units of pRBCs received during the 12-week period prior to the Baseline (Day 1) visit, must not be on a regular transfusion program, must be RBC transfusion-free for at least ≥ 4 weeks prior to randomization, and must not be scheduled to start a regular
6. hematopoietic stem cell transplantation within 9 months.
7. NTDT subjects: Subjects must have Hb ≤10.0 g/dL at Screening; the screening Hb sample must be collected 7 to 28 days prior to randomization. Hb values within 21 days post-transfusion will be excluded.
8. ECOG performance score of 0 to 1
9. Female subjects must not be pregnant, or breastfeeding and be highly unlikely to become pregnant. Male subjects must be unlikely to impregnate a partner.

Exclusion Criteria:

1. Diagnosis of α-thalassemia (e.g., hemoglobin H [HbH]) or hemoglobin S (HbS)/ β thalassemia.
2. Body mass index (BMI) <17.0 kg/m2 or a total body weight <45 kg; or BMI >35 kg/m2
3. Subjects with known active hepatitis A, hepatitis B, or hepatitis C, with active or acute event of malaria, or who are known to be positive for human immunodeficiency virus (HIV).
4. Stroke requiring medical intervention ≤24 weeks prior to randomization.
5. Platelet count >1000 × 109/L.
6. Participated in another clinical study of an investigational agent (or device) within 30 days or 5-half-lives of date of informed consent, whichever is longer, or is currently participating in another study.
7. For Subjects on iron chelation therapy (ICT) at the time of ICF signing, initiation of ICT less than 24 weeks before the predicted randomization date.
8. Prior exposure to sotatercept or luspatercept, IMR-687, or gene therapy within 6 months prior to randomization (Day 1).
9. Subjects who have major organ damage

Contacts and Locations

Locations

Denmark

Herlev Hospital
Herlev, Hovedstaden, Denmark, 2730

France

Hôpital Necker-Enfants Malades
Paris, France, 75015

Institut Universitaire du Cancer de Toulouse Oncopole
Toulouse cedex 9, Haute-Garonn, France, 31059

Hôpital Edouard Herriot
Lyon Cedex 03, Rhone, France, 69437

Georgia

National Center of Surgery
Tbilisi, Georgia, 0159

Medinvest - Institute of Hematology and Transfusiology
Tbilisi, Georgia, 0186

M. Zodelava Hematology Centre
Tbilisi, Borjomi, Georgia, 0112

Greece

Aghia Sofia General Children's Hospital
Athens, Attica, Greece, 11527

Laiko General Hospital of Athens
Athens, Attica, Greece, 11527

Ippokrateio General Hospital of Thessaloniki
Thessaloníki, Central Macedonia, Greece, 54642

University General Hospital of Patras
Patra, Peloponnese, Greece, 26504

Israel

Emek Medical Center
Afula, Israel, 18101

Rambam Health Care Campus
Haifa, Haifa District, Israel, 3109601

Hadassah University Hospital Ein Kerem
Jerusalem, Jerusalem District, Israel, 9112001

The Galilee Medical Center
Nahariya, Northern District, Israel, 2210001

Italy

Azienda Ospedaliera Universitaria - Università degli Studi della Campania Luigi Vanvitelli
Orbassano, Turin, Italy, 10043

Azienda Ospedaliera Giuseppe Brotzu
Orbassano, Turin, Italy, 10043

Lebanon

Chronic Care Center
Hazmiyeh, Lebanon, 213

Malaysia

Hospital Sultanah Aminah Johor Bharu
Johor Bahru, Johor, Malaysia, 80100

Hospital Sultanah Bahiyah
Alor Setar, Kedah, Malaysia, 05460

Hospital Pulau Pinang
George Town, Penang, Malaysia, 10450

Hospital Raja Permaisuri Bainun
Ipoh, Perak, Malaysia, 30450

Hospital Queen Elizabeth - Kota Kinabalu
Kota Kinabalu, Sabah, Malaysia, 88586

Hospital Umum Sarawak
Kuching, Sarawak, Malaysia, 93586

Morocco

Hôpital d'Enfants Rabat
Rabat, Morocco, 10100

Netherlands

Amsterdam Universitair Medische Centra - Academisch Medisch Centrum
Amsterdam, North Holland, Netherlands, 1105 AZ

Tunisia

Centre Hôpital Universitaire Farhat Hached
Sousse, Tunisia, 4000

Centre National de Greffe de la Moelle Osseuse
Tunis, Tunisia, 1006

Hospital Aziza Othmana
Tunis, Tunisia, 1008

Turkey

Hacettepe Üniversitesi
Ankara, Turkey, 06230

Ege Universitesi Tip Fakultesi
Izmir, Turkey, 35100

Akdeniz Üniversitesi
Mersin, Icel, Turkey, 33110

Mersin Üniversitesi Tıp Fakültesi
Mersin, Icel, Turkey, 33110

United Kingdom

University College London Hospitals NHS Foundation Trust
London, England, United Kingdom, NW1 2PG

Whittington Health NHS Trust

London, England, United Kingdom, N19 5NF
Manchester University NHS Foundation Trust
Manchester, England, United Kingdom, M13 9WL

Investigators

Study Director: Kenneth Attie, MD Imara, Inc.

Study Documents (Full-Text)

Documents provided by Imara, Inc.

Study Protocol [PDF] March 15, 2021

Statistical Analysis Plan [PDF] October 14, 2021

More Information

Responsible Party:	Imara, Inc.
ClinicalTrials.gov Identifier:	NCT04411082
Other Study ID Numbers:	IMR-BTL-201 2019-002989-12
Last Verified:	June 2022

Human Subjects Protection Review Board Status: Approved

Studies a U.S. FDA-regulated Drug Product: Yes

Studies a U.S. FDA-regulated Device Product: No

Study Results

Participant Flow

Recruitment Details	
Pre-assignment Details	

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo	NTDT High Dose	NTDT Low Dose	NTDT Placebo	Total (Not public)
Arm/Group Description	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	
Period Title: **Overall Study**							
Started	29	25	20	24	12	12	122
Completed	18	16	16	10	8	6	74
Not Completed	11	9	4	14	4	6	48

Baseline Characteristics

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo	NTDT High Dose	NTDT Low Dose	NTDT Placebo	Total
Arm/Group Description	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	

Overall Number of Baseline Participants		29	25	20	24	12	12	122
▼ Baseline Analysis Population Description		Safety Analysis Set						
Age, Continuous Mean (Standard Deviation) Unit of measure: Years	Number Analyzed	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants
		31.7 (12.06)	30.0 (9.95)	31.3 (8.57)	34.1 (12.64)	28.5 (8.21)	36.0 (9.56)	31.9 (10.69)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants
	Female	15 51.72%	15 60%	9 45%	10 41.67%	6 50%	8 66.67%	63 51.64%
	Male	14 48.28%	10 40%	11 55%	14 58.33%	6 50%	4 33.33%	59 48.36%
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants
	American Indian or Alaska Native	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
	Asian	5 17.24%	7 28%	4 20%	4 16.67%	3 25%	4 33.33%	27 22.13%
	Native Hawaiian or Other Pacific Islander	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
	Black or African American	1 3.45%	0 0%	0 0%	0 0%	1 8.33%	0 0%	2 1.64%
	White	19 65.52%	17 68%	14 70%	17 70.83%	7 58.33%	6 50%	80 65.57%
	More than one race	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
	Unknown or Not Reported	4 13.79%	1 4%	2 10%	3 12.5%	1 8.33%	2 16.67%	13 10.66%
Region of Enrollment Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants
United Kingdom		1 3.45%	0 0%	0 0%	2 8.33%	0 0%	1 8.33%	4 3.28%
Malaysia		4 13.79%	6 24%	4 20%	3 12.5%	3 25%	2 16.67%	22 18.03%
Greece		9 31.03%	2 8%	1 5%	5 20.83%	0 0%	2 16.67%	19 15.57%
Lebanon		0 0%	4 16%	3 15%	0 0%	1 8.33%	0 0%	8 6.56%
Netherlands		0 0%	0 0%	0 0%	2 8.33%	0 0%	1 8.33%	3 2.46%
Turkey		3 10.34%	5 20%	7 35%	1 4.17%	0 0%	0 0%	16 13.11%
Morocco		1 3.45%	1 4%	0 0%	2 8.33%	0 0%	2 16.67%	6 4.92%
Denmark		3 10.34%	0 0%	2 10%	0 0%	0 0%	0 0%	5 4.1%
Italy		0 0%	0 0%	0 0%	0 0%	1 8.33%	1 8.33%	2 1.64%
Georgia		0 0%	2 8%	1 5%	3 12.5%	1 8.33%	1 8.33%	8 6.56%
Israel		2 6.9%	2 8%	2 10%	1 4.17%	0 0%	0 0%	7 5.74%
France		2 6.9%	1 4%	0 0%	0 0%	2 16.67%	2 16.67%	7 5.74%
Tunisia		4 13.79%	2 8%	0 0%	5 20.83%	4 33.33%	0 0%	15 12.3%
BMI	Number	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants

Mean (Standard Deviation) Unit of measure: kg/m2	Analyzed							
		22.900 (3.2252)	21.252 (2.2874)	22.699 (2.9968)	22.031 (3.5415)	21.1320 (3.5047)	21.9120 (3.5638)	22.0873 (3.1573)
Serum Ferritin Mean (Standard Deviation) Unit of measure: micrograms per liter	Number Analyzed	29 participants	25 participants	20 participants	24 participants	12 participants	12 participants	122 participants
		1724.4 (1857.66)	3449.1 (5093.24)	1793.3 (1844.72)	981.4 (951.29)	945.8 (962.09)	447.8 (222.32)	1726.69 (2740.18)

Outcome Measures

1. Primary Outcome

Title:	IMR-687 Safety and Tolerability
Description:	Incidence and severity of Adverse Events Incidence and severity of Serious Adverse Events
Time Frame:	Baseline to Week 40

Outcome Measure Data ✓ Notes

Analysis Population Description
Safety Analysis set

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo	NTDT High Dose	NTDT Low Dose	NTDT Placebo
Arm/Group Description:	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	29	25	20	24	12	12
Measure Type: Count of Participants Unit of Measure: participants						
Row Title						
Treatment emergent Adverse Events	25 86.21%	22 88%	15 75%	18 75%	12 100%	6 50%
Treatment emergent Adverse Event related to study drug	19 65.52%	15 60%	8 40%	11 45.83%	7 58.33%	4 33.33%
Grade 3 or greater treatment emergent Adverse Event	4 13.79%	9 36%	2 10%	4 16.67%	1 8.33%	1 8.33%

2. Secondary Outcome

Title:	TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥33% Hematological Improvement From Week 12 to Week 24
Description:	Proportion of patients with ≥33% hematological improvement (as measured by reduced transfusion burden) from Week 12 to Week 24 compared to the 12 weeks prior to Baseline (Day 1)
Time Frame:	Baseline to Week 24

Outcome Measure Data ✓ Notes

Analysis Population Description
Per Protocol Analysis

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo

Arm/Group Description:	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	21	18	18
Measure Type: Count of Participants Unit of Measure: participants	2 9.52%	1 5.56%	2 11.11%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	TDT High Dose, TDT Low Dose, TDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.99
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

3. Secondary Outcome

Title:	NTDT Patients: Proportion of Subjects With an Increase From Baseline of Hb at Week 12 to Week 24 in the Absence of Transfusions.
Description:	Proportion of subjects with an increase from baseline of ≥1.0 g/dL in mean Hb values at Week 12 to Week 24 in the absence of transfusions.
Time Frame:	Baseline to Week 24

Outcome Measure Data Notes

Analysis Population Description
Per protocol analysis

Arm/Group Title	NTDT High Dose	NTDT Low Dose	NTDT Placebo
Arm/Group Description:	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	15	10	10
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%	0 0%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	NTDT High Dose, NTDT Low Dose, NTDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.99
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

4. Secondary Outcome

Title:	NTDT Patients: Proportion of Subjects With an Increase From Baseline of ≥3% in Mean HbF Values at Week 12 to Week 24 in Absence of Transfusions
▼ Description:	Proportion of subjects with an increase from baseline of ≥3% in mean HbF values at Week 12 to Week 24 in absence of transfusions NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	Baseline to Week 24

▼ Outcome Measure Data ✓ Notes

▼ Analysis Population Description
Per Protocol Analysis

Arm/Group Title	NTDT High Dose	NTDT Low Dose	NTDT Placebo
▼ Arm/Group Description:	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	11	5	8
Measure Type: Count of Participants Unit of Measure: participants	1 9.09%	1 20%	0 0%

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Group Selection	NTDT High Dose, NTDT Low Dose, NTDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.99
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

5. Secondary Outcome

Title:	TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥33% Hematological Improvement From Week 24 to Week 36
▼ Description:	Proportion of patients with ≥33% hematological improvement from Week 24 to Week 36 compared to the 12 weeks prior to Baseline (Day 1)
Time Frame:	Baseline to Week 36

▼ Outcome Measure Data ✓ Notes

▼ Analysis Population Description
Per Protocol Analysis

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo
▼ Arm/Group Description:	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	16	13	15
Measure Type: Count of Participants Unit of Measure: participants	0 0%	1 7.69%	1 6.67%

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Group Selection	TDT High Dose, TDT Low Dose, TDT Placebo

	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.4839
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

6. Secondary Outcome

Title:	TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥50 % Hematological Improvement From Week 12 to Week 24
▼ Description:	Proportion of patients with ≥50% hematological improvement from Week 12 to Week 24 compared to the 12 weeks prior to Baseline (Day 1)
Time Frame:	Baseline to Week 24

▼ Outcome Measure Data ✓ Notes

▼ Analysis Population Description
Per Protocol Analysis

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo
▼ Arm/Group Description:	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	21	18	18
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%	2 11.11%

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Group Selection	TDT High Dose, TDT Low Dose, TDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2065
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

7. Secondary Outcome

Title:	TDT Patients: Reduction in Red Blood Cell (RBC) Transfusion Burden With ≥50% Hematological Improvement From Week 24 to Week 36
▼ Description:	Proportion of patients with ≥50% hematological improvement from Week 24 to Week 36 compared to the 12 weeks prior to Baseline (Day 1)
Time Frame:	Baseline to Week 36

▼ Outcome Measure Data ✓ Notes

▼ Analysis Population Description
Per Protocol Analysis

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo

Arm/Group Description:	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	16	13	15
Measure Type: Count of Participants Unit of Measure: participants	0 0%	1 7.69%	1 6.67%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	TDT High Dose, TDT Low Dose, TDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4839
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

8. Secondary Outcome

Title:	NTDT Patients: Proportion of Subjects With an Increase From Baseline of Hb at Week 24 to Week 36 in the Absence of Transfusions
Description:	Proportion of subjects with an increase from baseline of ≥1.0 g/dL in mean Hb values at Week 24 to Week 36 in the absence of transfusions.
Time Frame:	Baseline to Week 36

Outcome Measure Data Notes

Analysis Population Description
Per Protocol Analysis

Arm/Group Title	NTDT High Dose	NTDT Low Dose	NTDT Placebo
Arm/Group Description:	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	12	9	8
Measure Type: Count of Participants Unit of Measure: participants	1 8.33%	1 11.11%	0 0%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	NTDT High Dose, NTDT Low Dose, NTDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.99
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

9. Secondary Outcome

Title:	NTDT: Proportion of Subjects With an Increase From Baseline of ≥3% in Mean HbF Values at Week 24 to Week 36 in Absence of Transfusions
▼ Description:	Proportion of subjects with an increase from baseline of ≥3% in mean HbF values at Week 24 to Week 36 in absence of transfusions NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	Baseline to Week 36

▼ Outcome Measure Data ✓ Notes

▼ Analysis Population Description
Per Protocol Analysis

Arm/Group Title	NTDT High Dose	NTDT Low Dose	NTDT Placebo
▼ Arm/Group Description:	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Participants Analyzed	8	6	7
Measure Type: Count of Participants Unit of Measure: participants	1 12.5%	0 0%	0 0%

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Group Selection	NTDT High Dose, NTDT Low Dose, NTDT Placebo
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	>0.99
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Adverse Events

Time Frame	10 months
Adverse Event Reporting Description	
Source Vocabulary Name for Table Default	[Not specified]
Collection Approach for Table Default	Systematic Assessment

Arm/Group Title	TDT High Dose	TDT Low Dose	TDT Placebo	NTDT High Dose	NTDT Low Dose
▼ Arm/Group Description	TDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	TDT Placebo NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT High dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	NTDT Low dose NOTE : An Arm/Group Description is shorter than the Arm/Group Title.

All-Cause Mortality

	TDT High Dose	TDT Low Dose	TDT Placebo	NTDT High Dose	NTDT Low Dose
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/29 (0%)	0/25 (0%)	0/20 (0%)	0/24 (0%)	0/12 (0%)

Serious Adverse Events

	TDT High Dose		TDT Low Dose		TDT Placebo		NTDT High Dose		NTDT Low Dose	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	1/29 (3.45%)		3/25 (12%)		1/20 (5%)		3/24 (12.5%)		0/12 (0%)	
Hepatobiliary disorders										
Cholelithiasis †	0/29 (0%)	0	0/25 (0%)	0	0/20 (0%)	0	1/24 (4.17%)	1	0/12 (0%)	0
Infections and infestations										
COVID19 †	0/29 (0%)	0	2/25 (8%)	2	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0
Liver abscess †	0/29 (0%)	0	1/25 (4%)	1	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0
Lower Respiratory Tract Infection †	0/29 (0%)	0	0/25 (0%)	0	0/20 (0%)	0	1/24 (4.17%)	1	0/12 (0%)	0
Pneumonia †	0/29 (0%)	0	1/25 (4%)	1	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0
Injury, poisoning and procedural complications										
Carbon Monoxide Poisoning †	0/29 (0%)	0	0/25 (0%)	0	1/20 (5%)	1	0/24 (0%)	0	0/12 (0%)	0
Lower Limb Fracture †	0/29 (0%)	0	0/25 (0%)	0	0/20 (0%)	0	1/24 (4.17%)	1	0/12 (0%)	0
Transfusion Reaction †	1/29 (3.45%)	1	0/25 (0%)	0	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0
Musculoskeletal and connective tissue disorders										
Back Pain †	1/29 (3.45%)	1	0/25 (0%)	0	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0
Skin and subcutaneous tissue disorders										
Rash †	1/29 (3.45%)	1	0/25 (0%)	0	0/20 (0%)	0	0/24 (0%)	0	0/12 (0%)	0

† Indicates events were collected by systematic assessment.

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

	TDT High Dose		TDT Low Dose		TDT Placebo		NTDT High Dose		NTDT Low Dose	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	25/29 (86.21%)		22/25 (88%)		15/20 (75%)		18/24 (75%)		12/12 (100%)	
Blood and lymphatic system disorders										
Anemia †	0/29 (0%)		1/25 (4%)		1/20 (5%)		2/24 (8.33%)		2/12 (16.67%)	
Gastrointestinal disorders										
Abdominal Distension †	2/29 (6.9%)		0/25 (0%)		1/20 (5%)		0/24 (0%)		0/12 (0%)	
Abdominal Pain †	2/29 (6.9%)		2/25 (8%)		0/20 (0%)		0/24 (0%)		1/12 (8.33%)	
Abdominal Pain Upper †	2/29 (6.9%)		1/25 (4%)		1/20 (5%)		3/24 (12.5%)		3/12 (25%)	
Diarrhoea †	4/29 (13.79%)		1/25 (4%)		2/20 (10%)		1/24 (4.17%)		2/12 (16.67%)	
Nausea †	11/29 (37.93%)		6/25 (24%)		1/20 (5%)		5/24 (20.83%)		1/12 (8.33%)	
Vomitting †	1/29 (3.45%)		0/25 (0%)		0/20 (0%)		3/24 (12.5%)		2/12 (16.67%)	
General disorders										
Fatigue †	1/29 (3.45%)		0/25 (0%)		0/20 (0%)		3/24 (12.5%)		2/12 (16.67%)	
Infections and infestations										
COVID19 †	1/29 (3.45%)		3/25 (12%)		0/20 (0%)		3/24 (12.5%)		0/12 (0%)	

Gastroenteritis †	3/29 (10.34%)	0/25 (0%)	0/20 (0%)	0/24 (0%)	0/12 (0%)
Nervous system disorders					
Dizziness †	5/29 (17.24%)	5/25 (20%)	2/20 (10%)	1/24 (4.17%)	0/12 (0%)
Headache †	10/29 (34.48%)	10/25 (40%)	7/20 (35%)	5/24 (20.83%)	2/12 (16.67%)
Respiratory, thoracic and mediastinal disorders					
Cough †	2/29 (6.9%)	0/25 (0%)	2/20 (10%)	1/24 (4.17%)	1/12 (8.33%)

† Indicates events were collected by systematic assessment.

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact

Name/Official Title:	Rahul Ballal
Organization:	Imara, Inc.
Phone:	617-206-2020
Email:	rballal@imaratx.com