

Study registered at the country of origin: Specify

Date of registration in national regulatory agency

### A Phase 3B, open-label, single-arm, rollover study to evaluate long-term safety in subjects who have participated in other luspatercept (ACE-536) clinical trials

Protocol number

ACE-536-LTFU-001

Type of registration: Justify

Primary sponsor: Country of origin

N/A

01/11/2019

Acronym

Acronym

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Primary registry identifying number

LBCTR2019100218

MOH registration number

43106/2019

Study registered at the country of origin

Type of registration

Date of registration in national regulatory

01/11/2019

Prospective

**Primary sponsor** Celgene Corporation

Date of registration in primary registry

22/05/2024

**Public title** 

A Phase 3B, open-label, single-arm, rollover study to evaluate longterm safety in subjects who have participated in other luspatercept (ACE-536) clinical trials

Scientific title

A Phase 3B, open-label, single-arm, rollover study to evaluate longterm safety in subjects who have participated in other luspatercept

(ACE-536) clinical trials

Brief summary of the study: English

This is a Phase 3b, open-label, single-arm, rollover study for subjects who have participated in other luspatercept (ACE-536) clinical trials.

The primary objective is to evaluate the long-term safety (including progression to acute myeloid leukemia (AML) and/or other malignancies/pre-malignancies) of luspatercept in subjects who have participated in other luspatercept clinical trials. Another objective is to follow subjects for overall survival.

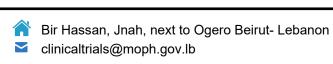
Brief summary of the study: Arabic

ب، الدراسة المفتوحة ذات الذراع الواحد، والانتقال إلى الأشخاص الذين شاركوا في تجارب سريرية أخرى3دراسة مرحلة (ACE-536). و / أو الأورام الخبيئة الأخرى / ما) (AML)الهدف الأساسي هو تقييم السلامة طويلة الأجل (بما في ذلك التقدم إلى سرطان الدم النخاعي الحاد الأخرى. هدف آخر هو luspatercept في الموضوعات الذين شاركوا في التجارب السريرية luspatercept قبل الأورام الخبيثة) من متابعة الموضوعات للبقاء على قيد الحياة بشكل عام

Health conditions/problem studied: Specify

Prior participation on a clinical trial of luspatercept (ACE-536) in protocols eligible for participation in this study ACE-536-LTFU-001 with the following medical conditions:

- Myelodysplastic Syndrome (MDS)
- Beta (β)-thalassemia (THAL)





Myelofibrosis (MF)

In Lebanon, only patients with beta (β)-thalassemia (THAL) have participated in previuos clinical trial of luspatercept (ACE-536).

#### Interventions: Specify

Starting as soon as Day 1 of Dose 1 of the rollover protocol, and assessed by the investigator prior to every subsequent treatment dose, subjects may have the dose level increased in a stepwise manner:

- beyond the starting dose from last dose of luspatercept from the parent protocol up to the defined maximum treatment dose.
- beyond the starting dose of 1.0 mg/kg in case of subjects crossing over to luspatercept from placebo arm of the parent protocol up to the defined maximum treatment dose.

#### Key inclusion and exclusion criteria: Inclusion criteria

Subjects must meet ALL the following criteria to be enrolled in this study:

- 1. Subject is ≥ 18 years at the time of signing the informed consent form (ICF).
- 2. Subject is willing and able to adhere to the study visit schedule and other protocol requirements.
- 3. Subject has been participating in a luspatercept trial and continues to fulfill all the requirements of the parent protocol and the subject has been either:
- a. Assigned to luspatercept treatment, continues to receive clinical benefit in the opinion of the investigator and should continue to receive luspatercept treatment, OR
- b. Assigned to placebo arm in the parent protocol (at the time of unblinding or in follow-up) and should cross over to luspatercept treatment. OR
- c. Assigned to the Follow-up Phase of the parent protocol, previously treated with luspatercept or placebo in the parent protocol who shall continue into Long-term Post-treatment Follow-up Phase in the rollover study until the follow-up commitments are met (unless requirements are met as per parent protocol to crossover to luspatercept treatment).
- 4. Subject understands and voluntarily signs an informed consent document prior to any study-related assessments or procedures being conducted.
- 5. Subject demonstrates compliance, as assessed by the investigator, with the parent study protocol requirements.
- 6. Applies to on treatment subjects only- females of childbearing potential (FCBP) defined as a sexually mature woman who:
- 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy, or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (ie, has had menses at any time in the preceding 24 consecutive months) and must:
- a. Have two negative pregnancy tests as verified by the investigator prior to starting study therapy. She must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the subject practices true abstinence\* from heterosexual contact.
- b. Either commit to true abstinence\* from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with highly effective, contraception without interruption, 35 days prior to starting investigational product (IP), during the study therapy (including dose interruptions), and for 84 days after discontinuation of study therapy.
- 7. Applies to on treatment subjects only- Male subjects must:
- a. Practice true abstinence\* (which must be reviewed on a monthly basis) or agree to use a condom during sexual contact with a pregnant female or a female of childbearing potential while participating in the study, during dose interruptions and for at least 84 days following investigational product discontinuation even if he has undergone a successful vasectomy.

Key inclusion and exclusion criteria: Gender

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

Key inclusion and exclusion criteria: Age maximum

### Key inclusion and exclusion criteria: Exclusion criteria

The presence of any of the following will exclude a subject from enrollment:

- 1. Applies to on treatment subjects only- Concomitant use of any medications/procedures that are prohibited in the parent luspatercept protocol.
- 2. Subject has met one or more criteria for study treatment discontinuation as stipulated in the parent luspatercept protocol.
- 3. First luspatercept transition visit into rollover study > 21 days after end of study (EOS) visit (last dose/visit in case of no EOS visit) of the parent luspatercept study with the exception of those subjects already in the Post-treatment Follow up Phase from the parent study. Note-Subject with current dose delays from the parent protocol during the Transition Phase, will continue in the rollover protocol regardless of the delay.
- 4. Applies to on treatment subjects only- Pregnant or breastfeeding females.
- 5. Subject has any significant medical condition, laboratory abnormality, psychiatric illness, or is considered vulnerable by local regulations (eg, imprisoned or institutionalized) that would prevent the subject from participating in the study.





Type of intervention: Specify type

Trial scope: Specify scope

Study design: Masking

Open (masking not used)

Year of authorization

Study design: Specify purpose

Study design: Specify assignment

IMP has market authorization: Specify

Month of authorization

Study phase

- 6. Subject has any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study.
- 7. Subject has any condition that confounds the ability to interpret data from the study.

#### Type of study

Interventional

Type of intervention

Pharmaceutical

Trial scope

Safety

**Study design: Allocation** N/A: Single arm study

Study design: Control

N/A

Study design: Purpose

Treatment

Study design: Assignment

Single

IMP has market authorization

No

Name of IMP

Luspatercept (ACE-536)

Type of IMP

Others

#### Pharmaceutical class

Luspatercept is a recombinant fusion protein consisting of a modified form of the extracellular domain (ECD) of the human activin receptor IIB (ActRIIB) linked to the human immunoglobulin G1 fragment crystallizable (IgG1 Fc) domain. Luspatercept is a homodimeric protein comprised of 2 disulfide-linked polypeptide chains, each with 335 amino acids. Each polypeptide chain contains 3 sites for N-linked glycosylation (total of 6N- linked glycosylation sites per molecule). Peptide mapping and oligosaccharide analysis of luspatercept confirms the presence of highly branched N-linked glycans, typical of a recombinant protein produced in Chinese hamster ovary cells.

#### Therapeutic indication

Myelodysplastic Syndrome (MDS); Beta (β)-thalassemia (THAL); Myelofibrosis (MF);

Only patients with beta (β)-thalassemia (THAL) are applicable in Lebanon

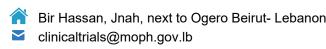
### Therapeutic benefit

Luspatercept acts as a ligand trap for Growth Differentiation Factor 11 (GDF11) and other TGF- $\beta$  family ligands to suppress Smad2/3 signaling. In nonclinical experiments, luspatercept has been shown to bind with high affinity to some TGF- $\beta$  ligands (eg, GDF11, GDF8, BMP6, and activin B) but substantially less, or not at all, to others (eg, BMP9 and activin A). The mechanism of action of luspatercept is independent from that of erythropoietin. While erythropoietin stimulates proliferation and differentiation of early erythroid progenitors, luspatercept promotes stimulation of the later, maturation phase of erythroblast differentiation and maturation in the bone marrow.

Study model

N/A

Study model: Explain model





Time perspective: Explain time perspective

Study model: Specify model

N/A

N/A

N/A

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

Not applicable

Target sample size

742

Date of first enrollment: Type

Anticipated

Date of study closure: Type

Anticipated

Recruitment status

Recruiting

Date of completion

Actual enrollment target size

Date of first enrollment: Date

19/02/2020

Date of study closure: Date

30/06/2027

**Recruitment status: Specify** 

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 partial date of birth will only be collected. 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

Admin comments



**Trial status** 

Approved

Secondary Identifying Numbers		
Full name of issuing authority	Secondary identifying number	
Food and Drug Administration	IND 112562	

### **Sources of Monetary or Material Support**

Name

Celgene Corporation

### **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	009611612 500	zog_az@mct- cro.com	Regional Manager
Scientific	Ali Taher	Chronic Care Center, Hazmieh, Lebanon	Lebanon	009613755 669	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	NA	
American university of Beirut	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	30/09/2019	Michele Abi saad	cccmas@chroniccare.org.lb	05 455 103	



Countries of Recruitment
Name
Lebanon
Bulgaria
Greece
Italy
Thailand
United Kingdom
United States of America
Belgium
Malaysia
Turkey
Australia
France
Germany
Canada
Netherlands
Spain
Sweden
Tunisia
Taiwan

Health Conditions or Problems Studied			
Condition	Code	Keyword	
Thalassemia	Thalassaemia (D56)	Thalassemia	



Interventions				
Intervention	Description	Keyword		
ACE-536	every 3 weeks (Q3W):1.0 mg/kg or same dose as last dose of parent protocol in case IP dose modifications occurred	Treatment Phase		

Primary Outcomes					
Name	Time Points	Measure			
Adverse events (AEs)	Enrollment to 42 days post last dose	Type, frequency, severity of AEs, relationship of treatment emergent adverse events to luspatercept			
Development of other malignancies/pre-malignancies	Enrollment to Long-term Post-treatment Follow-up	Number and percentage of subjects developing other malignancies/premalignancies			
Progression to high/very high risk myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) (MDS and myelofibrosis [MF] only). Not applicable for Lebanon patient population consists of B-Thal patients only.	Number and percentage of subjects progressing to high/very high risk MDS or AML	Enrollment to LTPTFU			

Key Secondary Outcomes				
Name	Time Points	Measure		
Overall survival	Enrollment to Long-term Post-treatment Follow-up	Time from date of randomization until death from any cause		



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	