CMBG453B12301 Study of Efficacy and Safety of MBG453 in Combination With Azacitidine in Subjects With Intermediate, High or Very High Risk Myelodysplastic Syndrome (MDS) as Per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2)

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Main Information

Primary registry identifying number
LBCTR2020094590

Protocol number
CMBG453B12301

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
Novartis Pharmaceuticals

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
06/06/2022

Date of registration in national regulatory agency

Public title
CMBG453B12301 Study of Efficacy and Safety of MBG453 in Combination With Azacitidine in Subjects With Intermediate, High or Very High Risk Myelodysplastic Syndrome (MDS) as Per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2)

Acronym
CMBG453B12301

Scientific title
A Randomized, Double-blind, Placebo-controlled Phase III Multi-center Study of Azacitidine With or Without MBG453 for the Treatment of Patients With Intermediate, High or Very High Risk Myelodysplastic Syndrome (MDS) as Per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2)

Acronym

Brief summary of the study: English
This is a Phase III multi-center, randomized, two-arm parallel-group, double-blind, placebo-controlled study of MBG453 or placebo added to azacitidine in adult subjects with intermediate, high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2) who have an indication for treatment with azacitidine in first-line setting and are not eligible for intensive chemotherapy or hematopoietic stem cell transplantation (HSCT) according to medical judgment by the investigator.

The purpose of the current study is to assess clinical effects of MBG453 in combination with azacitidine in adult subjects with IPSS -R intermediate, high, very high risk MDS and CMML-2.

Brief summary of the study: Arabic

دراسة متعددة المراكز، عشوائيّة التوزيع، مزدوجة التعمية، مرتكزة على المقارنة بدواء وهمي، في المرحلة الثالثة حول دواء أزاسيتيدين مع أو بدون MBG 453 لعلاج المرضى المصابين بمتلازمة خلل التنسّج النقوي العالية الخطورة أو ذات الخطورة العالية جداً وفقاً للنظام الدولي المنقحّ لتسجيل النتائج (IPSS-R) 2 أو بسرطان الدم الوحيديّ النقويّ المزمن-

Health conditions/problem studied: Specify

•Myelodysplastic Syndromes
•Leukemia, Myelomonocytic, Chronic

Interventions: Specify

•Drug: MBG453
A dose of MBG453 800 mg will be administered intravenously (IV) every 4 weeks (Q4W).

•Drug: Azacitidine
A dose of Azacitidine 75 mg/m2 will be administered IV or subcutaneously (SC) on Day 1-7, or Day 1-5, 8 and 9.

•Drug: Placebo
A dose of Placebo 800 mg will be administered intravenously every 4 weeks (Q4W).

Key inclusion and exclusion criteria: Inclusion criteria

Inclusion Criteria:
•Signed informed consent must be obtained prior to participation in the study
•Age ≥ 18 years at the date of signing the informed consent form

•Morphologically confirmed diagnosis of myelodysplastic syndrome (MDS) based on WHO 2016 classification (Arber et al 2016) by local investigator assessment with one of the following Prognostic Risk Categories, based on the revised International Prognostic Scoring System (IPSS-R):
◦Very high (> 6 points)
◦High (> 4.5 - ≤ 6 points)
◦Intermediate (> 3 - ≤ 4.5 points) Or Morphologically confirmed diagnosis of Chronic Myelomonocytic Leukemia -2 based on WHO 2016 classification (Arber et al 2016) by local investigator assessment with WBC < 13 x 109/L

•Indication for azacitidine treatment according to the investigator, based on local standard medical practice and institutional guidelines for treatment decisions
•Not eligible at time of screening for intensive chemotherapy according to the investigator, based on local standard medical practice and institutional guidelines for treatment decisions, including assessment of individual clinical factors such as age, comorbidities and performance status
•Not eligible at time of screening for hematopoietic stem cell transplantation (HSCT) according to the investigator, based on local standard medical practice and institutional guidelines for treatment decisions, including assessment of individual clinical factors such as age, comorbidities, performance status, and donor availability
•Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2

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

99

Key inclusion and exclusion criteria: Exclusion criteria

•Prior exposure to TIM-3 directed therapy at any time. Prior therapy with immune checkpoint inhibitors (e.g, anti-CTLA4, anti-PD-1, anti-PD-L1, or anti-PD-L2), cancer vaccines is allowed except if the drug was administered within 4 months prior to randomization
•Previous first-line treatment for intermediate, high, very high risk myelodysplastic syndromes (based on IPSS-R) or CMML with any antineoplastic agents including for example chemotherapy, lenalidomide and hypomethylating agents (HMAs) such as decitibine and azacitidine. However, previous treatment with hydroxyurea or leukopheresis to reduce WBC count is allowed prior to randomization.
•Investigational treatment received within 4 weeks or 5 half-lives of this investigational treatment, whatever is longer, prior to randomization. In case of a checkpoint inhibitor: a minimal interval of 4 months prior to randomization is necessary to allow randomization.
•Subjects with Myelodysplastic syndrome (MDS) based on 2016 WHO classification (Arber et al 2016) with revised International Prognostic Scoring System (IPSS-R) ≤ 3
•Diagnosis of acute myeloid leukemia (AML) including acute promyelocytic leukemia and extra-medullary acute myeloid leukemia, primary or secondary myelofibrosis based on WHO 2016 classification (Arber et al 2016)
•Diagnosis of therapy related myeloid neoplasms based on WHO 2016 classification (Arber et al 2016)
•History of organ or allogeneic hematopoietic stem cell transplant

Other protocol-defined Inclusion/Exclusion Criteria may apply.

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
Blinded (masking used)

Study design: Control
Placebo

Study phase
3

Study design: Purpose
Treatment

Study design: Specify purpose
N/A

Study design: Assignment
Parallel

Study design: Specify assignment
N/A

IMP has market authorization
No

IMP has market authorization: Specify

Name of IMP
MBG453

Year of authorization

Month of authorization

Type of IMP
Immunological

Pharmaceutical class
humanized monoclonal antibody against human TIM-3

Therapeutic indication
Patients with:
Myelodysplastic Syndromes or with chronic Leukemia Myelomonocytic

Therapeutic benefit
The primary objective of this study is to compare overall survival (OS) in the MBG453 plus azacitidine arm versus placebo plus azacitidine arm where OS is the time from randomization until death due to any cause.

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 without DNA

Biospecimen description

Samples will be shipped to covance central laboratory and BMA will be

Target sample size

4

Actual enrollment target size

1

Date of first enrollment: Type

Actual

Date of first enrollment: Date

05/07/2021

Date of study closure: Type

Actual

Date of study closure: Date

25/11/2027

Recruitment status

Recruiting

Recruitment status: Specify

Date of completion

29/07/2022

IPD sharing statement plan

Yes

IPD sharing statement description

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent expert panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT04266301?term=MBG&draw=2&rank=2&view=record

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical trials.gov	NCT04266301

Sources of Monetary or Material Support

Name
Novartis Pharmaceuticals

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Ali Bazarbachi	Beirut	Lebanon	961-1-350000 ext 5800	bazarbac@aub.edu.lb	American University of Beirut Medical Center
Scientific	Hind Khairallah	Beirut	Lebanon	9611512002 ext 271	hind.khairallah@fattal.com.lb	Khalil Fattal et Fils

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
American UNiversity of Beirut medical Center	Ali Bazarbachi	Hematology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	31/08/2020	Fuad Zyiadeh	fz05@aub.edu.lb	9611350000 ext 5445

Countries of Recruitment

Name
Lebanon
Australia
Austria
Belgium
Oman
Saudi Arabia
Czech Republic
Finland
France
Japan
Singapore
Spain
Switzerland
Taiwan
Thailand

Health Conditions or Problems Studied

Condition	Code	Keyword
MDS	Myelodysplastic syndrome, unspecified (D46.9)	MDS
CMML 2	Chronic monocytic leukaemia (C93.1)	CMML2

Interventions

Intervention	Description	Keyword
Informed consent, IMP administration, questionnaire , Bone marrow aspirate, Lab tests	Informed consent, IMP administration, questionnaire , Bone marrow aspirate, Lab tests	Informed consent, IMP administration, questionnaire , Bone marrow aspirate, Lab tests

Primary Outcomes

Name	Time Points	Measure
Overall Survival	5 years	5 years

Key Secondary Outcomes

Name	Time Points	Measure
Time to definitive deterioration of fatigue using Functional Assessment of Cancer Therapy (FACIT)-Fatigue score	5 years	5 years
Red Blood Cell transfusion-free intervals	5 years	5 years
Percent of subjects with at least 3 point confirmed improvement from baseline in FACIT-fatigue scoresscore	5 years	5 years
Percent of subjects with at least 10 point confirmed improvement from baseline in physical functioning using European Or ganization for Research and Treatment of Cancer's Core Quality of Life Questionnaire	5 years	5 years
Percentage of subjects with either CR, or mCR, or PR, or HI in each treatment arm according to International Working Group for MDS	5 years	5 years
Progression Free Survival (PFS)	5 years	5 years
Percentage of subjects with stable disease in each treatment arm according to International Working Group for MDS (IWG-MDS) as per investigator assessment	5 years	5 years

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