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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)

10/09/2025 20:23:29

Main Information	
Primary registry identifying number	Protocol number
LBCTR2020094590	CMBG453B12301
MOH registration number	
Study registered at the country of origin	Study registered at the country of origin: Specify
Yes	
Type of registration	Type of registration: Justify
Prospective	N/A
Date of registration in national regulatory agency	
Primary sponsor	Primary sponsor: Country of origin
Novartis Pharmaceuticals	Novartis Pharmaceuticals
Date of registration in primary registry	Date of registration in national regulatory agency
15/07/2021	
Public title	Acronym
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)	CMBG453B12301
Scientific title	Acronym
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)	
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	

Brief summary of the study: Arabic

-R intermediate, high, very high risk MDS and CMML-2.

دراسة متعددة المراكز، عشوائيَّة التوزيع، مزدوجة التعمية، مرتكزة على المقارنة بدواء و همي، في المرحلة الثالثة حول دواء أز استيدين مع أو 453 بدون MBG لعلاج المرضى المصابين بمتلازمة خلل التنسج النقوي العالية الخطورة أو ذات الخطورة العالية جداً وفقًا للنظام الدولي المنقَّحُ لتسجيل النتائج (IPSS-R) 2أو بسرطان الدم الوحيديّ النَّقويّ الَّمزِ من-

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Health conditions/problem studied: Specify

Myelodysplastic Syndromes

·Leukemia, Myelomonocytic, Chronic

Interventions: Specify

•Drua: 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

18

Key inclusion and exclusion criteria: Age minimum

Key inclusion and exclusion criteria: Age maximum

Key inclusion and exclusion criteria: Specify gender

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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

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Type of intervention	Type of intervention: Specify type
Pharmaceutical	N/A
Trial scope	Trial scope: Specify scope
Therapy	N/A
Study design: Allocation	Study design: Masking
Randomized controlled trial	Blinded (masking used)
Study design: Control	Study phase
Placebo	3
Study design: Purpose	Study design: Specify purpose
Treatment	N/A
Study design: Assignment	Study design: Specify assignment
Parallel	N/A
IMP has market authorization	IMP has market authorization: Specify
No	
Name of IMP	Year of authorization Month of authorization
MBG453	
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 arm versus placebo plus azacitidine arm where OS is the time from randomi: any cause.	
Study model	Study model: Explain model
N/A	N/A
Study model: Specify model	
N/A	
Time perspective	Time perspective: Explain time perspective
N/A	N/A
Time perspective: Specify perspective N/A	
Target follow-up duration	Target follow-up duration: Unit

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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.

Number of groups/cohorts

Biospecimen retention Biospecimen description Samples without DNA Samples will be shipped to covance central laboratory and BMA will be Target sample size Actual enrollment target size 4 Date of first enrollment: Type Date of first enrollment: Date Anticipated 29/10/2020 Date of study closure: Type Date of study closure: Date 25/11/2027 Anticipated **Recruitment status Recruitment status: Specify** Pending Date of completion 29/07/2022 IPD sharing statement plan IPD sharing statement description Novartis is committed to sharing with qualified external Yes 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

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.e du.lb	American University of Beirut Medical Center
Scientific	Hind Khairallah	Beirut	Lebanon	961151200 2 ext 271	hind.khairallah@f attal.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

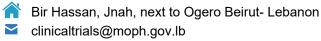
Ethics Review				
Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	31/08/2020	Fuad Zyiadeh	fz05@aub.edu.lb	9611350000 ext 5445



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