A Study of Sabatolimab in Combination With Azacitidine and Venetoclax in High or Very High Risk MDS Participants

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Main Information

Primary registry identifying number
LBCTR2022055033

Protocol number
CMBG453B12203

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
A Study of Sabatolimab in Combination With Azacitidine and Venetoclax in High or Very High Risk MDS Participants

Acronym
STIMULUS-MDS3

Scientific title
A Single-arm, Open-label, Phase II Study of Sabatolimab in Combination With Azacitidine and Venetoclax in Adult Participants With High or Very High Risk Myelodysplastic Syndromes (MDS) as Per IPSS-R Criteria

Acronym
STIMULUS-MDS3

Brief summary of the study: English
The purpose of the study is to find out if the new drug sabatolimab when given in combination with azacitidine and venetoclax, is safe and has beneficial effects in participants with high or very high risk myelodysplastic syndrome (MDS) who are not suitable for treatment with intensive chemotherapy or a stem-cell transplant (HSCT).

Brief summary of the study: Arabic
الغرض من الدراسة هو معرفة ما إذا كان الدواء الجديد ساباتوليماب عند إعطائه بالاشتراك مع أزاسيتيدين وفينيتوكلاكس، آمنًا وله آثار مفيدة لدى المشاركين الذين يعانون من متلازمة خلل التنسّج النقوي العالية الخطورة أو ذات الخطورة العالية جدًا غير المناسبين للعلاج الكيميائي المكثف أو لزرع الخلايا الجذعيّة.

Health conditions/problem studied: Specify
Myelodysplastic Syndromes (MDS)

Interventions: Specify
- Drug: sabatolimab
Sabatolimab will be administered at a low dose (Safety run-in (Part 1) cohort 1) or a high dose (Safety run-in (Part 1) cohort 2 and Expansion (Part 2)) via i.v. infusion over 30 minutes on Day 8 of every treatment cycle.

- Drug: azacitidine
A standard dose of azacitidine will be given subcutaneously or intravenously every day for seven consecutive days on days 1-7 of a confirmed

treatment cycle. In keeping with standard clinical practice, the alternative schedules for five consecutive days on days 1-5, followed by a two day break, then two consecutive days on days 8-9 will be permitted (alternative schedule).

- Drug: venetoclax
Venetoclax film-coated tablets will be administered at a dose of 400 mg orally or corresponding reduced dose for concomitant use with P-gp inhibitors or moderate or strong CYP3A4 inhibitors, once a day, from C1D1 to C1D14 during the treatment cycle. No ramp-up for venetoclax is necessary.

Key inclusion and exclusion criteria: Inclusion criteria

1- Signed informed consent must be obtained prior to participation in the study
2- Age ≥ 18 years at the date of signing the informed consent form (ICF)
3- Morphologically confirmed diagnosis of myelodysplastic syndrome (MDS) based on 2016 WHO 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) (Greenberg et al 2012):
    - Very high (> 6 points)
    - High (> 4.5-6 points)
4- Not immediately eligible for hematopoietic stem-cell transplantation (HSCT) or intensive chemotherapy at the time of screening due to individual clinical factors such as age, comorbidities and performance status, donor availability (de Witte et al 2017)
5- 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

1- Prior exposure to TIM-3 directed therapy or any BCL-2 inhibitor (including venetoclax) at any time
2- Prior therapy with immune check point inhibitors (e.g. anti-CTLA4, anti-PD-1, anti-PD-L1, or anti-PD-L2) or cancer vaccines is not allowed if the last dose of the drug was administered within 4 months prior to start of treatment
3- Previous first-line treatment for very high risk or high risk myelodysplastic syndromes (based on IPSS-R,Greenberg et al 2012 and Arber et al, 2016) with any antineoplastic agents, approved or investigational, including for example chemotherapy, lenalidomide and hypomethylating agents (HMAs) such as decitabine or azacitidine However, a one single cycle of HMAs treatment only started prior to enrollment is allowed.
4- Live vaccine administered within 30 days prior to start of treatment
5- Current use or use within 14 days prior to start of treatment of systemic steroid therapy (> 10 mg/day prednisone or equivalent) or any immunosuppressive therapy. Topical, inhaled, nasal, ophthalmic steroids are allowed. Replacement therapy, steroids given in the context of a transfusion, are allowed and not considered a form of systemic treatment
6- History of severe hypersensitivity reactions to any ingredient of study drug(s) (azacitidine, venetoclax or sabatolimab) or monoclonal antibodies (mAbs) and/or their excipients
7- Participants with Myelodysplastic syndrome (MDS) based on 2016 WHO classification (Arber et al, 2016) with revised International Prognostic Scoring System (IPSS-R) ≤ 4.5

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

N/A

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

Other

Study design: Specify assignment

Sequential

IMP has market authorization

IMP has market authorization: Specify

No

Name of IMP

Sabatolimab

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

humanized monoclonal antibody against human TIM-3

Therapeutic indication

Myelodysplastic Syndrome (MDS)

Therapeutic benefit

The purpose of the study is to find out if the new drug sabatolimab when given in combination with azacitidine and venetoclax, is safe and has beneficial effects in participants with high or very high risk myelodysplastic syndrome (MDS) who are not suitable for treatment with intensive chemotherapy or a stem-cell transplant (HSCT).

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 Labcorp laboratories

Target sample size

3

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

20/07/2022

Date of study closure: Type

Anticipated

Date of study closure: Date

06/12/2025

Recruitment status

Pending

Recruitment status: Specify

Date of completion

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.
This trial data is currently available according to the process described on www.clinicalstudydatarequest.com.

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT04812548?term=CMBG453B12203&draw=2&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
ClinicalTrials.gov	NCT04812548

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 3 612434	bazarbac@aub.edu.lb	American University of Beirut Medical Center
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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/Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	17/03/2022	Fuad Zyiadeh	fz05@aub.edu.lb	+961 1 350 000 ext:5445

Countries of Recruitment

Name
Australia
Belgium
France
Germany
Greece
Hungary
Italy
Spain
United States of America
Lebanon

Health Conditions or Problems Studied

Condition	Code	Keyword
Myelodysplastic Syndrome	Myelodysplastic syndrome, unspecified (D46.9)	MDS

Interventions

Intervention	Description	Keyword
Informed consent, IMP administration, questionnaire, Lab tests	Informed consent, IMP administration, questionnaire, Lab tests	Informed consent, IMP administration, questionnaire, Lab tests

Primary Outcomes

Name	Time Points	Measure
Incidence of dose limiting toxicities (DLTs) (Safety run-in patients only)	From Cycle 1 Day 8 to end of Cycle 2 (Cycle = 28 Days)	Assessment of tolerability of MBG in combination with venetoclax and azacitidine
Percentage of participants (receiving 800mg sabatolimab) achieving complete remission (CR) per investigator assessment	Throughout study completion, up to 3 years	This endpoint will assess Complete Remission (CR) Rate of participants from Cohort 2 of Part 1 and Part 2 according to Investigator assessment per modified IWG-MDS - Cheson 2006 criteria. CR is defined as follows: bone marrow blasts <=5%, hemoglobin level ≥ 10 g/dL, platelets count ≥ 100*10^9/L, neutrophils count ≥ 1.0*10^9/L, absence of blasts in peripheral blood.

Key Secondary Outcomes

Name	Time Points	Measure
Percentage of subjects achieving a complete remission (CR) + morphologic complete remission (mCR): Safety run-in (Part 1) and Expansion (Part 2)	Throughout study completion, an average of 3 years	Assessing the durability of complete remission (CR) or morphologic complete remission (mCR) rate (defined as the proportion of participants with best overall response of either CR or mCR)
Overall Response Rate (ORR) of participants who achieved hematologic improvement (HI) or better as best response	Throughout study completion, an average of 3 years	The percentage of participants achieving [CR + mCR + partial remission (PR) + hematologic improvement (HI)], per modified IWG-MDS Cheson 2006 criteria
Percentage of participants who are RBC/platelets transfusion independent	Continuously collected from start of treatment up to 3 years from last patient first treatment	Improvement in red blood cells (RBC)/platelets transfusion independence as per IWG-MDS by dose level
Duration of transfusion independence	Continuously collected from start of treatment up to 3 years from last patient first treatment	Transfusion independence as per IWG-MDS by dose level
Peak Serum Concentration (Cmax) MBG453	Continuously collected for patients during treatment with sabatolimab up to 150 days after last treatment	Maximal concentration of MBG453
Trough Serum Concentration (Cmin) MBG453	Continuously collected for patients during treatment with sabatolimab up to 150 days after last treatment	Concentration of sabatolimab prior to next dosing or after end of treatment
Anti-drug Antibody (ADA) prevalence at baseline and ADA incidence on-treatment by dose level	Continuously collected for patients during treatment with sabatolimab up to 150 days after last treatment	Immunogenicity of sabatolimab prior to sabatolimab exposure and during treatment
Duration of complete remission (CR)	Throughout study completion, an average of 3 years	Duration of CR is defined as time from first occurrence of CR to relapse from CR, progression or death due to any cause whichever occurs first
Time to complete remission(CR)/marrow complete remission (mCR)	Throughout study completion, an average of 3 years	Time to CR/mCR is defined as time from start of treatment to first occurrence of CR or mCR as per investigator assessment
Duration of CR/mCR	Throughout study completion, an average of 3 years	Duration of CR/mCR is defined as time from first occurrence of CR/mCR to relapse from CR, progression or death due to any cause whichever occurs first
Duration of response for participants who achieved hematologic improvement (HI) or better	Throughout study completion, an average of 3 years	The duration of response will be derived for participants treated with sabatolimab at the higher dose who achieve HI or better as per investigator assessment and is defined from the first occurrence of CR, mCR, PR or HI until relapse, progression or death due to any reason
Progression-Free Survival (PFS)	Throughout study completion, an average of 3 years	Time from start of treatment to disease progression (including transformation to acute leukemia per WHO 2016 classification), relapse from CR or death due to any cause, whichever occurs first
Leukemia-Free Survival (LFS)	Throughout study completion, an average of 3 years	Time from start of treatment to transformation to acute leukemia
Event-Free Survival (EFS)	Throughout study completion, an average of 3 years	Time from start of treatment to lack of reaching CR within the first 6 cycles, relapse from CR or death due to any cause, whichever occurs first
Overall Survival (OS)	Date of start of treatment to date of death due to any reason (for up to 3 years from last patient first treatment)	Time from start of treatment to death due to any cause
Changes in fatigue	Throughout the Expansion Phase, an average of 3 years	Changes in fatigue as measured by the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue for participants treated with sabatolimab at the higher dose of the expansion part only. Measurements are taken via scores from 0 (not at all) to 4 (very much). The higher the score, the better the Quality of Life.

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