A Study of MBG453 in Combination With Hypomethylating Agents in Subjects With IPSS-R Intermediate, High or Very High Risk Myelodysplastic Syndrome (MDS). (STIMULUS-MDS1)

ClinicalTrials.gov Identifier: NCT03946670

Recruitment Status : Recruiting
First Posted : May 13, 2019
Last Update Posted : January 14, 2020

See **Contacts and Locations**

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

Study Details | Tabular View | No Results Posted | Disclaimer
How to Read a Study Record

Study Description

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Brief Summary:

This Phase II is a multicenter, randomized, two-arm parallel-group, double-blind, placebo-controlled study of MBG453 or placebo added to hypomethylating agents (azacitidine or decitabine) in adult subjects with IPSS-R intermediate, high or very high risk myelodysplastic syndrome (MDS) not eligible for Hematopoietic Stem Cell Transplant (HSCT) or intensive chemotherapy.

Condition or disease	Intervention/treatment	Phase
Myelodysplastic Syndromes	Drug: MBG453 Drug: Placebo Drug: Hypomethylating agents	Phase 2

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	120 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Triple (Participant, Care Provider, Investigator)
Primary Purpose:	Supportive Care
Official Title:	A Randomized, Double-blind, Placebo-controlled Phase II Multi-center Study of Intravenous MBG453 Added to Hypomethylating Agents in Adult Subjects With Intermediate, High or Very High Risk Myelodysplastic Syndrome (MDS) as Per IPSS-R Criteria
Actual Study Start Date :	June 4, 2019
Estimated Primary Completion Date :	February 11, 2021
Estimated Study Completion Date :	August 3, 2023

Resource links provided by the National Library of Medicine NIH NLM

MedlinePlus related topics: Myelodysplastic Syndromes

Genetic and Rare Diseases Information Center resources: Myelodysplastic Syndromes

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: MBG453 + hypomethylating agents Patients will take MBG453 plus hypomethylating agents	Drug: MBG453 MBG453 will be administered i.v. Drug: Hypomethylating agents Decitabine will be administered i.v. Azacitidine will be administered i.v or s.c.
Placebo Comparator: Placebo + hypomethylating agents Patients will take placebo plus hypomethylating agents	Drug: Placebo Placebo will be administered i.v. Drug: Hypomethylating agents Decitabine will be administered i.v. Azacitidine will be administered i.v or s.c.

Outcome Measures

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Primary Outcome Measures :

1. Complete remission (CR) rate [Time Frame: 7 months after last patient first visit (LPFV)]

   Modified response criteria According to International Working Group (IWG) for Myelodysplastic syndromes (MDS) as per investigator assessment.

2. Progression Free Survival (PFS) [Time Frame: Up to 4 yrs after Last Patient First Visit (LPFV)]

Defined as time from randomization to disease progression (including transformation to leukemia per WHO 2016 classification), relapse from CR according to IWG-MDS or death due to any cause, whichever occurs first, as per investigator assessment

Secondary Outcome Measures :

1. Overall Suvival [Time Frame: Up to 4 years after last patient randomized]

   Time from randomization to death due to any cause

2. Leukemia-free survival [Time Frame: Up to 4 yrs after Last Patient First Visit (LPFV)]

   Time from randomization to ≥ 20% blasts in bone marrow/ peripheral blood (per WHO 2016 classification) or death due to any cause

3. Response Rate (CR/mCR/PR) [Time Frame: 7 months after Last Patient First Visit (LPFV)]

   Percentage of complete remission(CR)/marrow Complete Remission (mCR)/partial remission (PR) according to IWG-MDS as per investigator assessment

4. Duration of complete remission [Time Frame: Up to 4 yrs after Last Patient First Visit (LPFV)]

   Time from the date of the first documented CR to the date of first documented relapse from CR or death due to any cause, whichever occurs first

5. Time to complete remission [Time Frame: 7 months after Last Patient First Visit (LPFV)]

   Time from randomization to the first documented CR

6. Number of subjects who are RBC/platelets transfusion independent after randomization as per IWG-MDS [Time Frame: Up to 4 years after last randomized patient]

   Improvement in RBC/platelets transfusion independence

7. Percent of subjects who are red blood cells (RBC)/platelets transfusion independent after randomization as per IWG-MDS [Time Frame: Up to 4 years after last randomized patient]

   Improvement in RBC/platelets transfusion independence

8. Serum concentrations for MBG453 [Time Frame: At Day 8 of each cycle (1 cycle = 28 days) until cycle 6 and at day 8 of cycles 9, 12, 18 and 24, and up to 150 day of the safety follow up period]

Pharmacokinetics of MBG453 when given in combination with hypomethylating agents (HMA)

9. Immunogenicity of MBG453 when given in combination of hypomethylating agents
[Time Frame: Up to 4 years after Last Patient First Visit (LPFV)]

Anti-drug Antibody (ADA) prevalence at baseline and ADA incidence on-treatment

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

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 a myelodysplastic syndrome (MDS) based on 2016 WHO classification (Arber et al 2016) by investigator assessment with one of the following Prognostic Risk Categories, based on the International Prognostic Scoring System (IPSS-R):
   - Very high
   - High
   - Intermediate with at least ≥ 5% bone marrow blast
4. Not eligible for intensive chemotherapy

5. Not eligible for hematopoietic stem-cell transplantation (HSCT)
6. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2

Exclusion Criteria:

1. Prior exposure to TIM-3 directed therapy at any time. Prior therapy with immune check point inhibitors (e.g. anti-CTLA4, anti-PD-1, anti-PD-L1, or anti-PD-L2), cancer vaccines are allowed only if the last dose of the drug was administered more than 4 months prior to randomization.
2. Previous treatment for higher risk MDS with chemotherapy or other antineoplastic agents including lenalidomide and hypomethylating agent (HMAs) such as decitabine or azacitidine. However, previous treatment is permitted with hydroxyurea or leukopheresis.
3. History of severe hypersensitivity reactions to any ingredient of study drug(s) (azacitidine, decitabine or MGB453) or monoclonal antibodies (mAbs) and/or their excipients.
4. Current use or use within 14 days prior to randomization 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.
5. Investigational treatment for MDS received within 4 weeks prior to randomization. In case of a checkpoint inhibitor: 4 months minimum prior to randomization interval is necessary to allow enrollment.
6. Active autoimmune disease requiring systemic therapy (e.g.corticosteroids).
7. Live vaccine administered within 30 Days prior to randomization.

Other protocol-defined Inclusion/Exclusion may apply.

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03946670***

Contacts

Contact: Novartis Pharmaceuticals 1-888-669-6682 novartis.email@novartis.com

Contact: Novartis Pharmaceuticals +41613241111

Locations

▸ Show 49 study locations

Sponsors and Collaborators

Novartis Pharmaceuticals

Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

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Responsible Party:	Novartis Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT03946670 History of Changes
Other Study ID Numbers:	CMBG453B12201 2018-004479-11 (EudraCT Number)
First Posted:	May 13, 2019 Key Record Dates
Last Update Posted:	January 14, 2020
Last Verified:	January 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:	Yes
Supporting Materials:	Study Protocol Statistical Analysis Plan (SAP)
Access Criteria:	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.

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

Keywords provided by Novartis (Novartis Pharmaceuticals):

Phase II,	decitabine
MBG453	azacitidine
TIM-3	myelodysplastic syndrome (MDS)

Additional relevant MeSH terms:

Preleukemia	Neoplasms
Myelodysplastic Syndromes	Azacitidine
Syndrome	Decitabine
Disease	Antimetabolites, Antineoplastic
Pathologic Processes	Antimetabolites
Bone Marrow Diseases	Molecular Mechanisms of Pharmacological Action
Hematologic Diseases	Antineoplastic Agents
Precancerous Conditions	Enzyme Inhibitors