A Randomized, Double-Blind, Phase 3 Study Evaluating the Safety and Efficacy of Venetoclax in Combination with Azacitidine in Patients Newly Diagnosed with Higher-Risk Myelodysplastic Syndrome (Higher-Risk MDS)

Published: 23-09-2020
Last updated: 19-09-2024

This study has been transitioned to CTIS with ID 2023-507153-16-00 check the CTIS register for the current data. To assess the efficacy of venetoclax in combination with AZA compared to placebo with AZA in treatment-naive higher-risk MDS.

Ethical review	Approved WMO
Status	Pending
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON54378

Source
ToetsingOnline

Brief title
VERONA

Condition

- Leukaemias

Synonym
Myelodisplastic Syndrome (MDS), myelodysplasia

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie Deutschland GmbH & Co. KG
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Higher risk, Myelodysplastic Syndrome (MDS), Venetoclax

Outcome measures

Primary outcome

Overall Survival (OS)

Secondary outcome

- Complete remission (CR)

- Overall hematological improvement (HI) (HI-platelet, HI-neutrophil, or

HI-erythroid)

- Red blood cell (RBC) and platelet transfusion independence for subjects who

are transfusion dependent on RBC and/or platelet at baseline

- Change from baseline in fatigue, as measured by the Patient-Reported Outcomes

Measurement Information System (PROMIS)-Fatigue SF 7a

- Time to deterioration in physical functioning, as measured by the physical

functioning domain of EORTC QLQ-C30

- Overall response (OR) defined as CR + partial response (PR)

- Modified overall response (mOR) defined as CR + PR + marrow CR (mCR).

Study description

Background summary

Myelodysplastic Syndrome (MDS) is a group of disorders that gradually affect the ability of a person's bone marrow (semi-liquid tissue present in many bones like backbones) to produce normal blood cells. Some people with MDS have a risk of the disease progressing to acute myeloid leukemia (AML), and a risk of death from the disease itself.
Symptoms of MDS include fatigue, shortness of breath, unusual paleness due to anemia (low red blood cell count), easy or unusual bruising, and red spots just beneath the skin caused by bleeding. The purpose of this study is to see how safe and effective venetoclax and azacitidine (AZA) combination are when compared to AZA and a placebo (contains no medicine), in participants with newly diagnosed higher-risk MDS.

Study objective

This study has been transitioned to CTIS with ID 2023-507153-16-00 check the CTIS register for the current data.

To assess the efficacy of venetoclax in combination with AZA compared to placebo with AZA in treatment-naive higher-risk MDS.

Study design

This is a randomized, double-blind, placebo-controlled study.

Intervention

Participants in one arm will receive oral doses of venetoclax tablet and intravenous (infusion in the vein) or subcutaneous (given under the skin) AZA solution.
Participants in another arm will receive oral doses of placebo tablet and intravenous or subcutaneous AZA solution.

Study burden and risks

There may be higher treatment burden for participants in this trial compared to their standard of care. Participants will attend regular visits during the course of the study at a hospital or clinic. The effect of the treatment will be checked by medical assessments, blood and bone marrow tests, checking for side effects, and completing questionnaires.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult male or female, at least 18 years old. Diagnosis of MDS according to the 2016 WHO classification with presence of < 20% bone marrow blasts per bone marrow biopsy/aspirate at screening. Subject meets the following disease activity criteria:
* Overall IPSS-R score > 3 (intermediate, high, or very high; Appendix E);
* Eastern Cooperative Oncology Group (ECOG) performance status <= 2;
* HSCT eligible with no pre-arranged HSCT at the time of Study Day 1, or HSCT ineligible without plan for HSCT at the time of Study Day 1. No prior therapy for MDS with any hypomethylating agent (for example, azacitidine, decitabine), chemotherapy or allogeneic stem cell transplantation.

Exclusion criteria

No previous diagnosis of:
* Therapy-related MDS (t-MDS)
* MDS evolving from a pre-existing myeloproliferative neoplasm (MPN)
* MDS/MPN including chronic myelomonocytic leukemia (CMML), atypical chronic myeloid leukemia (aCML), juvenile myelomonocytic leukemia (JMML) and unclassifiable MDS/MPN
* No prior therapy for MDS with any hypomethylating agent (for example, azacitidine, decitabine), chemotherapy or allogeneic stem cell transplantation. Lenalidomide, anti-thymocyte globulin (ATG), and cyclosporin are also excluded as these are considered disease-modifying agents.
* No known active SARS-CoV-2 infection. If a subject has signs/symptoms of SARS-CoV-2 infection, they should undergo molecular (e.g., PCR) testing to rule out SARS-CoV-2 infection.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	16-11-2020
Enrollment:	13
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Brand name:	Azacitidine Accord
Generic name:	Azacitidine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Venclyxto
Generic name:	Venetoclax
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Vidaza
Generic name:	Azacitidine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-05-2021

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	07-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-507153-16-00
EudraCT	EUCTR2020-000744-55-NL
ClinicalTrials.gov	NCT04401748
CCMO	NL74107.056.20