A Retrospective Observational Cohort Study to Evaluate the Effectiveness of Azacitidine Monotherapy in Treatment-naive Patients With Intermediate, High, and Very High-risk Myelodysplastic Syndrome

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Study Finalised

Administrative details

EU PAS number

EUPAS38242

Study ID

49871

DARWIN EU® study

No

Study countries

United States

Study description

GS-US-545-5956: The primary objective of this study was to evaluate the effectiveness of azacytidine (AZA)(Vidaza® and other generic versions of Vidaza®) monotherapy as assessed by complete remission (CR) rates defined by the International Working Group (IWG) 2006 myelodysplastic syndrome (MDS) criteria in patients with intermediate, high, and very high-risk MDS.

Study status

Finalised

Research institutions and networks

Institutions

Gilead Sciences

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Institution | Pharmaceutical company

Contact details

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Primary lead investigator

Gilead Study Director

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 02/10/2020

Actual: 02/10/2020

Study start date
Planned: 01/01/2021

Actual: 15/03/2021

Date of final study report
Planned: 30/09/2022

Actual: 30/08/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Gilead Sciences

Study protocol

GS-US-545-5956-appendix-16.1.1-protocol_f-redact.pdf (1.53 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The primary objective of this study was to evaluate the effectiveness of AZA monotherapy as assessed by CR rates defined by the IWG 2006 MDS criteria in

patients with intermediate, high, and very high-risk MDS.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Retrospective study

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

AZACITIDINE

Medical condition to be studied

Myelodysplastic syndrome

Population studied

Short description of the study population

Patients aged 18 years or older receiving treatment with azacitidine for documented histological diagnosis of myelodysplastic syndrome (MDS) as per medical record documentation in the electronic health record (EHR) identified from the United States Oncology Network (USON) database between t between 01 January 2014 through 01 January 2020.

Inclusion Criteria:

1) Male or female ≥ 18 years of age.

2) Documented histological diagnosis of MDS defined as per medical record documentation in the EHR.

3) Documented Revised International Prognostic Scoring System (IPSS-R) MDS risk category of intermediate-, high-, or very high-risk.

4) Initiation of AZA monotherapy during the Study Index Period.

5) Received at least a single dose of treatment with AZA in line with US Prescribing information; the following dosing regimens were permitted:

a) AZA 75 mg/m2 on Days 1-7 of a monthly cycle.

b) AZA 75 mg/m2 on Days 1-5, 8-9 of a monthly cycle (5 days on, 2 days off on the weekend, 2 days on).

c) AZA 75 mg/m2 on Days 1-5 of a monthly cycle

6) Patients should not have received any antileukemic therapies for the treatment of MDS prior to the initiation of AZA. (Prior and concurrent therapy with hydroxyurea, oral etoposide, erythroid and/or myeloid growth factors, or any symptomatic treatment was allowed. Patients with MDS who received prior anticancer therapy from prior malignancies were permitted).

7) Patients had to have at least 1 posttreatment encounter in the EHR.

8) White blood cell (WBC) count ≤ 20 × 103/μL at the time of AZA initiation (use of hydroxyurea to reduce WBC prior to AZA initiation, as documented within the EHR was acceptable).

9) Adequate hepatic and renal function at the time of AZA initiation (within 30 days of index) as evidenced by the following documentation in the EHR: a) Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 5 × upper limit of normal (ULN).

b) Bilirubin ≤ 1.5 × ULN, or 3.0 × ULN and primarily unconjugated if patient had a documented history of Gilbert’s syndrome or genetic equivalent.

c) Serum creatinine ≤ 1.5 × ULN or calculated glomerular filtration rate (GFR) ≥

40 mL/min/1.73 m2

Exclusion Criteria:
1) Any prior antileukemic therapy including chemotherapy (excluding hydroxyurea or oral etoposide), targeted therapies, immunotherapy or radiotherapy.
2) Prior treatment with hypomethylating agents and/or low dose cytarabine. Prior treatment with lenalidomide or similar agents was permitted if treatment was utilized for symptomatic support (ie, anemia, red blood cell [RBC] transfusion dependence).
3) Patients participated in an interventional clinical trial during study observation period.
4) Previous hematopoietic stem cell transplant (SCT) within 6 months prior to initiation of AZA, active graft versus host disease (GVHD), or requiring transplant-related immunosuppression.
5) Patients who have had transformation of MDS into acute myeloid leukemia (AML) prior to initiation of AZA.
6) Known inherited or acquired bleeding disorders.
7) EHR documentation of clinical suspicion/radiological evidence of active central nervous system (CNS) involvement by leukemia.
8) Acute promyelocytic leukemia.
9) Second malignancy, except treated basal cell or localized squamous skin carcinomas, localized prostate cancer, or other malignancies for which patients were not on active anticancer therapy as defined in Exclusion Criterion 1.
10) Initiation of AZA treatment outside the approved label (except as described under the Inclusion Criterion 5); for example, in combination with other agents for the treatment of MDS.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Patients with myelodysplastic syndrome

Estimated number of subjects

382

Study design details

Outcomes

Complete remission rate, Real-world(rw) CR rate, objective response rate (ORR), rw-ORR, duration of CR (DCR), rw-DCR, duration of response (DOR), rw-DOR, Progression-Free Survival, time to next treatment, and overall survival.

Data analysis plan

Continuous variables were summarized by mean, standard deviation, median, 25% & 75% quantiles, minimum and maximum. Categorical variables were summarized by number and % of patients in each categorical definition including 95% confidence intervals. The Full Analysis Set (FAS) included all enrolled patients who took at least 1 dose of AZA. The Effectiveness Evaluable Analysis Set (EEAS) included all FAS patients who had at least 1 response assessment or died after the index date. The efficacy analyses (except DCR, rw-

DCR, DOR, and rw-DOR) was performed on the FAS. DCR and rw-DCR were evaluated using FAS patients who achieved a CR and rw-CR, respectively. DOR and rw-DOR were evaluated using FAS patients who achieved an OR and real-world objective response (rw-OR), respectively. Details of analytical comparison with magrolimab and AZA combination therapy trial (5F9005) data were included in the statistical analysis plan.

Documents

Study results

GS-US-545-5956-Synopsis_f-redact.pdf (1.07 MB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No