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

PURI
https://redirect.ema.europa.eu/resource/49871

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 institution and networks

Institutions

Gilead Sciences
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Institution

Pharmaceutical company

Contact details

Study institution contact
Gilead Study Director

Study contact

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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 data collection

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

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