SUPPLEMENTAL APPENDIX

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Pevonedistat plus azacitidine versus azacitidine alone in higher-risk MDS/CMML or AML with 20–30% marrow blasts

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Supplementary methods

Patient eligibility criteria

- Inclusion criteria:
    - Male or female patients aged 18 years or older
    - Morphologically confirmed diagnosis of myelodysplastic syndromes (MDS) or non-proliferative chronic myelomonocytic leukemia (CMML; i.e., with white blood cell [WBC] count <13,000/μL) or acute myeloid leukemia (AML) based on one of the following:

      French-American-British (FAB) Classifications [Bennett JM, et al. *Br J Haematol.* 1982;51(2):189-199].:

        - Refractory anemia with excess blasts (RAEB), defined as having 5–20% myeloblasts in the bone marrow
        - CMML with 10–19% myeloblasts in the bone marrow and/or 5–19% blasts in the blood

      OR

      World Health Organization (WHO) Classifications [Vardiman JW, et al. *Blood.* 2002;100(7):2292-302]:

        - RAEB-1, defined as having 5–9% myeloblasts in the bone marrow
        - RAEB-2, defined as having 10–19% myeloblasts in the bone marrow and/or 5–19% blasts in the blood
        - CMML-2, defined as having 10–19% myeloblasts in the bone marrow and/or 5–19% blasts in the blood
        - CMML-1 (although CMML-1 is defined as having <10% myeloblasts in the bone marrow and/or <5% blasts in the blood, these patients could enroll only if bone marrow blasts ≥5%)

- WHO-defined AML with 20–30% myeloblasts in the bone marrow and ≤30% myeloblasts in peripheral blood who were deemed by the investigator to be appropriate for azacitidine-based therapy

- All patients with MDS or CMML were also required to have one of the following Prognostic Risk Categories, based on the Revised International Prognostic Scoring System (IPSS-R) [Greenberg PL, et al. *Blood.* 2012;120(12):2454-2465]:
  - Very high (>6 points)
  - High (>4.5–6 points)
  - Intermediate (>3–4.5 points): a patient determined to be in the Intermediate Prognostic Risk Category was only allowable in the setting of ≥5% bone marrow myeloblasts
  - Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–2
- Patients with AML with 20–30% blasts were required to have a treatment-related mortality (TRM) score ≥4 for intensive induction chemotherapy, as calculated using the simplified model described by Walter and coworkers [Walter RB, et al. *J Clin Oncol.* 2011;29(33):4417-4423].

  Calculation of TRM score:
  - 0 for (age <61 years), +2 for (age 61–70 years), +4 for (age ≥71 years)
  - + 0 for (PS = 0), +2 for (PS = 1), +4 for (PS >1)
  - + 0 for (platelets <50 x 10^9/L), +1 for (platelets ≥50 x 10^9/L)
- Female patients who:
  - Were postmenopausal for at least 1 year before the screening visit, OR
  - Were surgically sterile, OR

        - If they were of childbearing potential, agreed to practice one highly effective method of contraception and one additional effective (barrier) method, at the same time, from the time of signing the informed consent through 4 months after the last dose of study drug, OR
        - Agreed to practice true abstinence, when this is in line with the preferred and usual lifestyle of the patient. (Periodic abstinence [e.g., calendar, ovulation, symptothermal, postovulation methods], withdrawal, spermicides only, and lactational amenorrhea were not acceptable methods of contraception. Female and male condoms should not be used together.)
    - Male patients, even if surgically sterilized (i.e., status postvasectomy), who:
        - Agreed to practice effective barrier contraception during the entire study treatment period and through 120 days (or if the drug has a very long half-life, for 90 days plus five half-lives) after the last dose of study drug, OR
        - Agreed to practice true abstinence, when this is in line with the preferred and usual lifestyle of the patient. (Periodic abstinence [e.g., calendar, ovulation, symptothermal, postovulation methods], withdrawal, spermicides only, and lactational amenorrhea were not acceptable methods of contraception. Female and male condoms should not be used together.)
    - Ability to undergo the study-required bone marrow sample collection procedures
    - Suitable venous access for the study-required blood sampling (i.e., including pharmacokinetic and pharmacodynamic sampling)
    - Clinical laboratory values within the following parameters (repeated within 3 days before the first dose of study drug if laboratory values used for

randomization were obtained more than 3 days before the first dose of study drug):

- Albumin >2.7 g/dL
- Total bilirubin ≤ the upper limit of the normal range (ULN) except in patients with Gilbert's syndrome. Patients with Gilbert's syndrome could enroll if direct bilirubin ≤1.5×ULN of the direct bilirubin
- Alanine aminotransferase and aspartate aminotransferase ≤2.5×ULN
- Creatinine clearance ≥50 mL/min
- Hemoglobin >8 g/dL. Patients could be transfused to achieve this value. Elevated indirect bilirubin due to posttransfusion hemolysis was allowed

- Voluntary written consent must have been given before performance of any study-related procedure not part of standard medical care, with the understanding that consent may be withdrawn by the patient at any time without prejudice to future medical care

- <u>Exclusion criteria:</u>
  - Previous treatment for higher-risk MDS/CMML or for AML with 20–30% blasts with chemotherapy or other antineoplastic agents including hypomethylating agents such as decitabine or azacitidine. Previous treatment was permitted with hydroxyurea and with lenalidomide, except that lenalidomide could not have been given within 8 weeks before the first dose of study drug
  - Acute promyelocytic leukemia as diagnosed by morphologic examination of bone marrow, by fluorescent *in situ* hybridization or cytogenetics of peripheral blood or bone marrow, or by other accepted analysis
  - Patients with AML with a WBC count >50,000/μL. Patients who were cytoreduced with leukapheresis or with hydroxyurea could be enrolled if they met the eligibility criteria

- Eligible for intensive chemotherapy and/or allogeneic stem cell transplantation. The reason a patient was not eligible for intensive chemotherapy and/or allogeneic stem cell transplantation could consist of one or more of the following factors:
    - Age >75 years
    - Comorbidities
    - Inability to tolerate intensive chemotherapy (e.g., patients with AML with 20–30% blasts and TRM ≥4)
    - Physician decision (e.g., lack of available stem cell donor)

  The reason a patient was not eligible had to be documented in the electronic case report form (eCRF)
- Patients with either clinical evidence of or history of central nervous system involvement by AML
- Any serious medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with the completion of study procedures or could limit expected patient survival to less than 6 months
- Treatment with any investigational products or participation in any interventional studies within 14 days before the first dose of any study drug
- Known hypersensitivity to pevonedistat or its excipients
- Known hypersensitivity to azacitidine or its excipients
- Active uncontrolled infection or severe infectious disease, such as severe pneumonia, meningitis, or septicemia
- Major surgery within 14 days before first dose or a scheduled surgery during the study period; insertion of a venous access device (e.g., catheter, port) was not considered major surgery
- Diagnosed or treated for another malignancy within 2 years before randomization or previously diagnosed with another malignancy and with any evidence of residual disease. Patients with nonmelanoma skin cancer or

carcinoma *in situ* of any type were not excluded if they had undergone resection

- Life-threatening illness unrelated to cancer
- Prothrombin time (PT) or activated partial thromboplastin time (aPTT) >1.5×ULN or active uncontrolled coagulopathy or bleeding disorder. Patients therapeutically anticoagulated with warfarin, direct thrombin inhibitors, direct factor Xa inhibitors, or heparin were excluded from enrollment
- Known human immunodeficiency virus (HIV) seropositive
- Known hepatitis B surface antigen seropositive, or known or suspected active hepatitis C infection. Note: Patients who had isolated positive hepatitis B core antibody (i.e., in the setting of negative hepatitis B surface antigen and negative hepatitis B surface antibody) had to have an undetectable hepatitis B viral load
- Known hepatic cirrhosis or severe pre-existing hepatic impairment
- Known cardiopulmonary disease defined as unstable angina, clinically significant arrhythmia, congestive heart failure (New York Heart Association Class III or IV, and/or myocardial infarction within 6 months before first dose, or severe pulmonary hypertension. As an example, well-controlled atrial fibrillation was not excluded whereas uncontrolled atrial fibrillation was excluded.
- Treatment with strong cytochrome P450 3A (CYP3A) inducers within 14 days before the first dose of pevonedistat
- Female patients who were lactating and breastfeeding or had a positive serum pregnancy test during the screening period or a positive urine pregnancy test on day 1 before first dose of study drug
- Female patients who intended to donate eggs (ova) during the course of this study or during the 4 months after receiving their last dose of study drug(s)

- Male patients who intended to donate sperm or father a child during the course of this study or during the 6 months after receiving their last dose of study drug(s)

Pevonedistat administration

Drug name: Pevonedistat (MLN4924; TAK924)

Dose: 20mg/m^2 on days 1, 3, and 5

Route: central or peripheral venous access

Type and volume of diluent; rate of administration: Patients received pevonedistat diluted with 5% dextrose or 0.9% saline in a 250 mL bag via a 60-minute IV infusion. The infusion could be slowed or stopped and restarted for any associated infusion-related reactions. All infusion times had to be recorded. The total time from drug reconstitution to end of infusion could not exceed 6 hours. The entire content of the pevonedistat IV bag was infused at a constant rate over 60 (±10) minutes. To ensure that all drug was administered, the infusion line was flushed with 0.9% saline or 5% dextrose immediately after administration.

Cycle length and number of cycles, or criteria for discontinuation: Patients received study drugs in 28-day cycles until unacceptable toxicity, relapse, transformation to AML (for patients with higher-risk MDS or CMML), or PD (for patients with AML with 20–30%), study termination, or discontinuation due to other reasons. A minimum of 6 cycles of treatment was strongly encouraged.

Premedications and concurrent medications: Antiplatelet agents (e.g., aspirin,

clopidogrel) and anticoagulants; myeloid growth factors (e.g., G-CSF, GM-CSF); platelet transfusion; red blood cell transfusion. See redacted protocol for more information.

Patient-monitoring parameters: Patients were monitored on dosing days of each cycle and additionally on days 8, 15, and 21 of cycle 1, at end of treatment, and every month for EFS and response follow up. See schedule of events in redacted protocol for full details.

Endpoints

- Primary endpoint: Event-free survival (EFS): time from randomization to the date of an EFS event (defined as death or transformation to AML in patients with higher-risk MDS or CMML, whichever occurred first, and defined as death in patients with AML with 20–30% blasts). For patients with higher-risk MDS or CMML, if a death event occurred prior to AML transformation, the date of death was used to determine EFS. If AML transformation occurred prior to death, the date of the transformation event was used to calculate EFS.
- Key secondary endpoint: overall survival (OS).
- Other secondary endpoints;
    - Six-month and 1-year survival rates.
    - Thirty-day and 60-day survival rates.
    - Time to AML transformation in patients with higher-risk MDS, patients with higher-risk CMML, and patients with higher-risk MDS/CMML.
    - Rate of complete remission (CR, in patients with higher-risk MDS or CMML, or AML with 20–30% blasts), CR+CR with incomplete blood count recovery (CRi) in patients with AML with 20–30% blasts, CR+marrow CR (in patients with higher-risk MDS or CMML), CR+partial remission (PR)+hematologic improvement (HI; in patients with higher-risk MDS or CMML), CR+marrow CR+PR (in patients with higher-risk MDS or CMML), CR+marrow CR+PR+HI (in patients with higher-risk MDS or CMML), overall response, overall response by cycle 6, and overall response 2. Overall response in patients with higher-risk MDS or CMML is defined as CR+PR; overall response in patients with AML with 20–30% blasts is defined as CR+CRi+PR. Overall response 2 in patients with higher-risk MDS or CMML is defined as CR+PR+HI; overall response 2 in patients with AML with 20–30% blasts is defined as CR+CRi+PR.

- Duration of CR (CR for higher-risk MDS or CMML, or AML with 20–30% blasts), CR+CRi for AML with 20–30% blasts, overall response (CR+PR for higher-risk MDS or CMML, CR+CRi+PR for AML with 20–30% blasts), and overall response 2 (CR+PR+HI for HR MDS or CMML, CR+CRi+PR for AML with 20–30% blasts).
- Rates of red blood cell (RBC) and platelet transfusion independence.
- Duration of RBC transfusion independence, platelet transfusion independence, and platelet and RBC transfusion independence.
- Time to first CR or PR or CRi (for patients with AML with 20–30% blasts).
- Rates of HI in patients with higher-risk MDS, patients with higher-risk MDS/CMML, and patients with higher-risk CMML.
- Patients who have inpatient hospital admission(s) related to higher-risk MDS or CMML (collected through transformation to AML or until initiation of subsequent therapy, whichever occurred first) or AML with 20–30% blasts (collected through initiation of subsequent therapy).
- Time to progressive disease (PD), relapse after CR (AML with 20–30% blasts), relapse after CR or PR (higher-risk MDS/CMML), or death.
- Health-related quality of life (HRQOL) assessed using the European Organization for Research and Treatment of Cancer quality of life questionnaire C30.
- Plasma concentration-time data for pevonedistat.
- ORR, EFS, and OS in patients who had *TP53* mutations, 17p deletions, and/or were determined to be in an adverse cytogenetic risk group in both treatment arms

After trial commencement, the co-primary endpoint of overall response rate (ORR) by cycle 6 was changed to a secondary endpoint. This was based on preliminary results from the

phase 2 P-2001 study that suggested that event-free survival (EFS) events more reliably reflected potential clinical benefit for patients.

Transfusion independence was defined as having no transfusion of red blood cells or platelets for a period of ≥8 weeks during the time period from initiation of study dosing through 30 days after the last dose of study drug.

Assessment timings

Bone marrow aspirates (BMAs) were performed on day 22 (+6 days) of cycles 2, 4, 6, and 9 and every third treatment cycle thereafter; in patients who achieved a CR, after cycle 4, BMAs were performed as clinically indicated. Patients attended the end-of-treatment (EOT) visit 30 days (+10 days) after the last dose of study drug or before the start of subsequent antineoplastic therapy if that occurred sooner. Following the EOT visit, patients with higher-risk MDS or CMML entered EFS follow-up, if their disease had not transformed to AML. Patients had monthly assessments including a physical exam, clinical blood tests, HRQOL assessments, hospitalization assessment, and disease assessment. Patients who discontinued study treatment without evidence of progression (i.e., PD or transformation to AML) had a BMA and hematology tests sent to the central laboratory at the time of suspected progression. Patients continued monthly EFS follow-up study visits until their disease transformed to AML or they started subsequent therapy. Patients who had started subsequent therapy had EFS follow-up but were not required to have monthly visits; at the time of suspected transformation to AML patients had a BMA and hematology tests with specimens sent to the central laboratory. Following the EOT visit, patients with AML with 20–30% blasts entered response follow-up if they had no evidence of PD and had not started subsequent therapy. Patients had monthly assessments including a physical exam, clinical blood tests, HRQOL assessments, hospitalization assessment, and disease assessment.

Patients who discontinued study treatment while not in CR and without evidence of PD had a BMA and hematology tests sent to the central laboratory at the time of suspected PD. Patients who discontinued treatment while in CR also had a BMA and hematology tests performed at the time of suspected relapse sent to the central laboratory. Patients continued monthly response follow-up visits until they relapsed from CR or met the criteria for PD. Following the EFS and response follow-up visits, or the EOT visit (for patients with higher-risk MDS or CMML who discontinued study treatment because of transformation to AML, or patients with AML with 20–30% blasts who discontinued study treatment because of PD), patients entered overall survival (OS) follow-up and were contacted every 3 months until death to document subsequent therapies and survival status.

Mutational analysis

Mutational analysis was conducted on 384 BMA samples collected at screening (270 higher-risk MDS; 24 higher-risk CMML; 90 AML with 20–30% blasts). DNA sequencing was performed using a 54-myeloid gene targeted panel on a duplex sequencing platform, which was developed to ensure variant bases were identified with support from both DNA strands and to allow for ultra-deep sequencing coverage of low variant allelic fractions (VAF <0.01%). Single-nucleotide variants, and insertions and deletions (indels) were identified using MuTect. A mutation curation methodology filtered the MuTect output such that only variants known to drive tumor growth, disease transformation, and progression were retained. Additional quality control steps eliminated false-positive mutations calls that resulted from alignment artifacts, such as slipped-strand mispairing in the *ASXL1* gene. A gene was designated “positive” for mutations if it had ≥1 nucleotide variant(s). FMS-like tyrosine kinase 3–internal tandem duplication mutations were further confirmed by polymerase chain reaction using the LeukoStrat® CDx test.

Cytogenetic analysis

BMA samples collected at screening were sent to the central laboratory for G-banded karyotyping and fluorescence *in situ* hybridization *TP53* deletion 17p analysis (ATM-TP53 Kreatech™ probe). Cytogenetic risk categories/subgroups were determined centrally by a certified pathologist per European LeukemiaNet guidelines [Döhner H, et al. *Blood.* 2017;129(4):424-447] for patients with AML with 20–30% blasts and per the IPSS-R for higher-risk MDS and higher-risk CMML patients, respectively [Greenberg PL, et al. *Blood*. 2012;120(12):2454-2465; Schanz J, et al. *J Clin Oncol.* 2012;30(8):820-829].

Statistical methods

There were two planned interim analyses (IAs) and one final analysis (FA). IA1 was planned to evaluate EFS for futility and re-assess the EFS event size for patients with higher-risk MDS for IA2. IA2 was the FA of EFS in the intent-to-treat (ITT) population and in the higher-risk MDS cohort (adaptive event size for IA2; n = 147 EFS events in the higher-risk MDS cohort). The FA evaluated OS. Since the prespecified number of approximately 202 OS events for FA occurred (based on blinded study data) close to the IA2, the IA2 and the FA were performed as a single analysis. Separate multiple hierarchical testing procedures, with the ITT population and the higher-risk MDS cohort as the primary analysis populations, were adopted to test the primary endpoint of EFS and the key secondary endpoint of OS, with OS then tested in other disease populations; each procedure had a total 1-sided alpha of 0.025 (Supplemental Figure 1).

There was one primary endpoint of EFS, and one key secondary endpoint of OS. The total number of patients was calculated on the basis of maintaining 83% power to test OS in patients with higher-risk MDS at a 1-sided alpha level of 0.025, as well as to ensure sufficient representation of patients with AML with 20–30% blasts. The study was also adequately powered to test EFS in patients in the ITT population and in the higher-risk MDS cohort, as well as to test OS in the ITT population. A total of approximately 450 patients,

including at least 350 patients with higher-risk MDS or CMML and at least 100 patients with AML with 20–30% blasts, were planned to be enrolled, with 320 patients with higher-risk MDS required to obtain 202 OS events. The minimal planned event size of 147 EFS events from patients with higher-risk MDS was based on an optimistic assumption of a hazard ratio (HR) of 0.585 (median EFS of 17.09 months in the combination arm vs 10 months in the azacitidine alone arm) with approximately 90% power at a 1-sided alpha of 0.025. The maximal planned event size of 249 EFS events from patients with higher-risk MDS was based on a relatively conservative assumption of an HR of 0.663 (median EFS of 15.08 months in the combination arm vs 10 months in the azacitidine alone arm) with approximately 90% power at a 1-sided alpha of 0.025. It was projected that the EFS event size from the ITT population would range approximately from 158 (approximately 92% power, 1-sided alpha = 0.025, HR = 0.585, median EFS of 22.22 months in the combination arm vs 13 months in the azacitidine alone arm) to 305 (approximately 95% power, 1-sided alpha = 0.025, HR = 0.663, median EFS of 19.61 months in the combination arm vs 13 months in the azacitidine alone arm). With the assumption of an HR of 0.663 for OS in patients with higher-risk MDS (median OS of 36.95 months in the combination arm vs 24.5 months in the azacitidine alone arm), 202 OS events provided approximately 83% power at a 1-sided alpha of 0.025. It was projected that approximately 280 OS events would occur in the ITT population, providing approximately 93% power to test OS in the ITT population.

Patient populations

The ITT population was defined as all patients who were randomized. Patients in this population were analyzed according to the treatment they were randomized to receive, regardless of any dosing errors.

The safety population was defined as all patients who received at least 1 dose of pevonedistat plus azacitidine or azacitidine alone. Patients were analyzed according to the actual treatment they received. Patients who received any dose of pevonedistat were

included in the combination arm, and patients who did not receive any dose of pevonedistat and received at least 1 dose of azacitidine were included in the azacitidine alone arm, regardless of their randomized treatment.

Supplemental tables

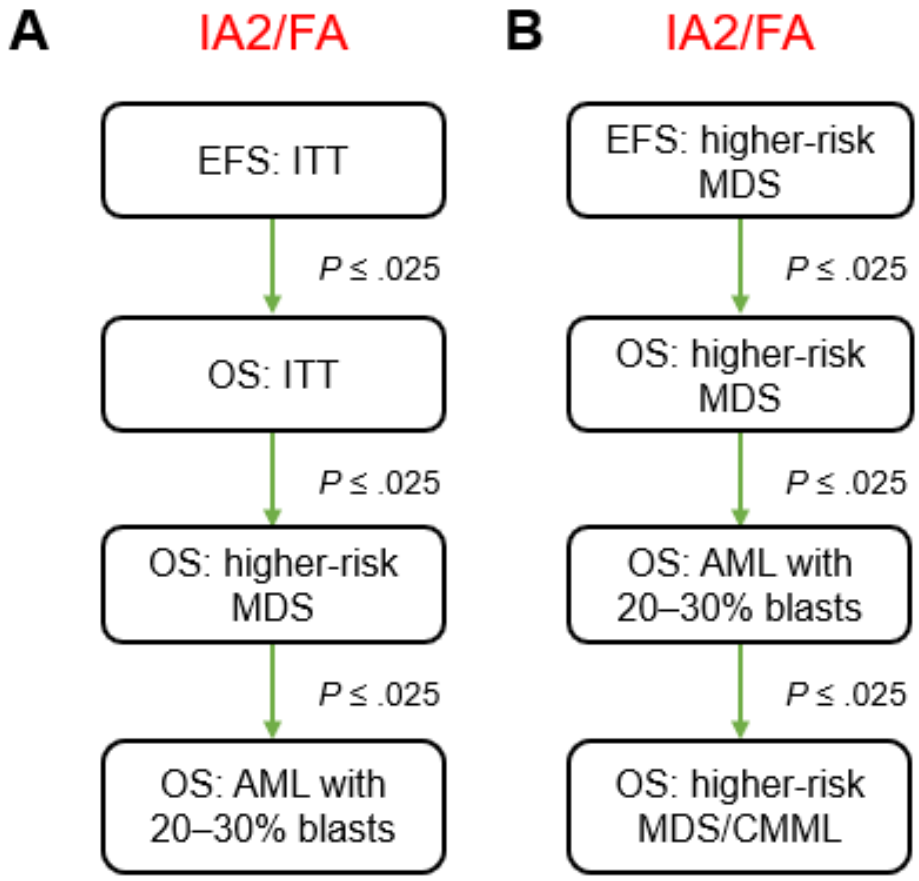
Supplemental Table 1. Reasons for discontinuation of treatment (both study drugs) in the ITT population and higher-risk MDS cohort for patients who had received ≤3 and ≤6 cycles

n (%)	Pevonedistat + azacitidine	Azacitidine alone
ITT population		
Received ≤3 cycles	**n = 227**	**n = 227**
Discontinued both study drugs	54 (24)	49 (22)
AE	31 (14)	21 (9)
Progression to AML	4 (2)	6 (3)
Progressive disease	11 (5)	5 (2)
Patient withdrawal	5 (2)	11 (5)
Other	3 (1)	6 (3)
Received ≤6 cycles		
Discontinued both study drugs	87 (38)	91 (40)
AE	38 (17)	28 (12)
Progression to AML	13 (6)	10 (4)
Progressive disease	18 (8)	18 (8)
Patient withdrawal	8 (4)	17 (7)
Other	10 (4)	18 (8)
Higher-risk MDS cohort	**n = 161**	**n = 163**
Received ≤3 cycles		
Discontinued both study drugs	36 (22)	37 (23)
AE	22 (14)	15 (9)
Progression to AML	4 (2)	5 (3)
Progressive disease	5 (3)	3 (2)
Patient withdrawal	2 (1)	8 (5)
Other	3 (2)	6 (4)
Received ≤6 cycles		
Discontinued both study drugs	60 (37)	65 (40)
AE	26 (16)	20 (12)
Progression to AML	13 (8)	9 (6)
Progressive disease	10 (6)	9 (6)
Patient withdrawal	5 (3)	13 (8)
Other	6 (4)	14 (9)

AE, adverse event; AML, acute myeloid leukemia; ITT, intent-to-treat; MDS, myelodysplastic syndromes.

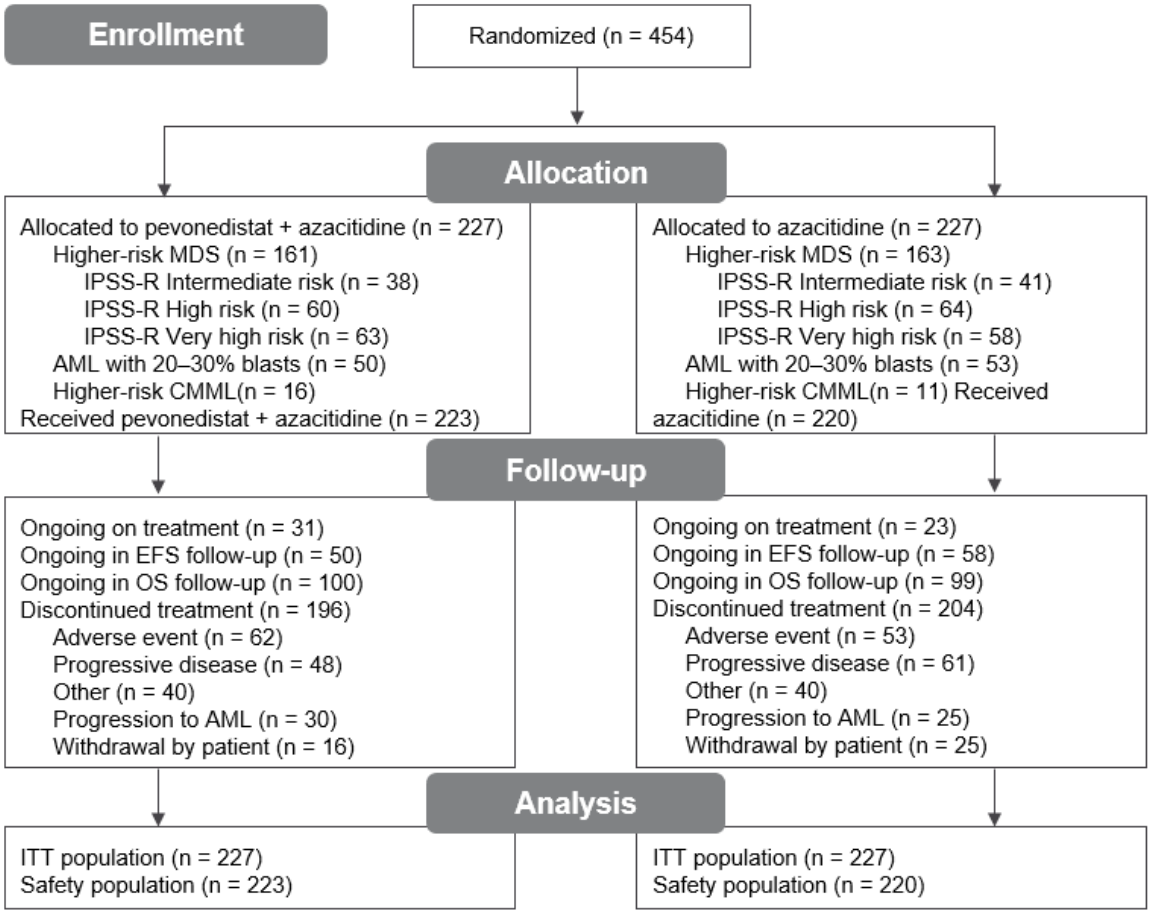
Supplemental figures

Supplemental Figure 1. Multiple hierarchical testing procedure at IA2/FA (A) with the overall ITT population as the primary analysis population and (B) with the higher-risk MDS cohort as the primary analysis population. AML, acute myeloid leukemia; CMML, chronic myelomonocytic leukemia; EFS, event-free survival; FA, final analysis; IA, interim analyses; ITT, intent-to-treat; MDS, myelodysplastic syndromes; OS, overall survival.

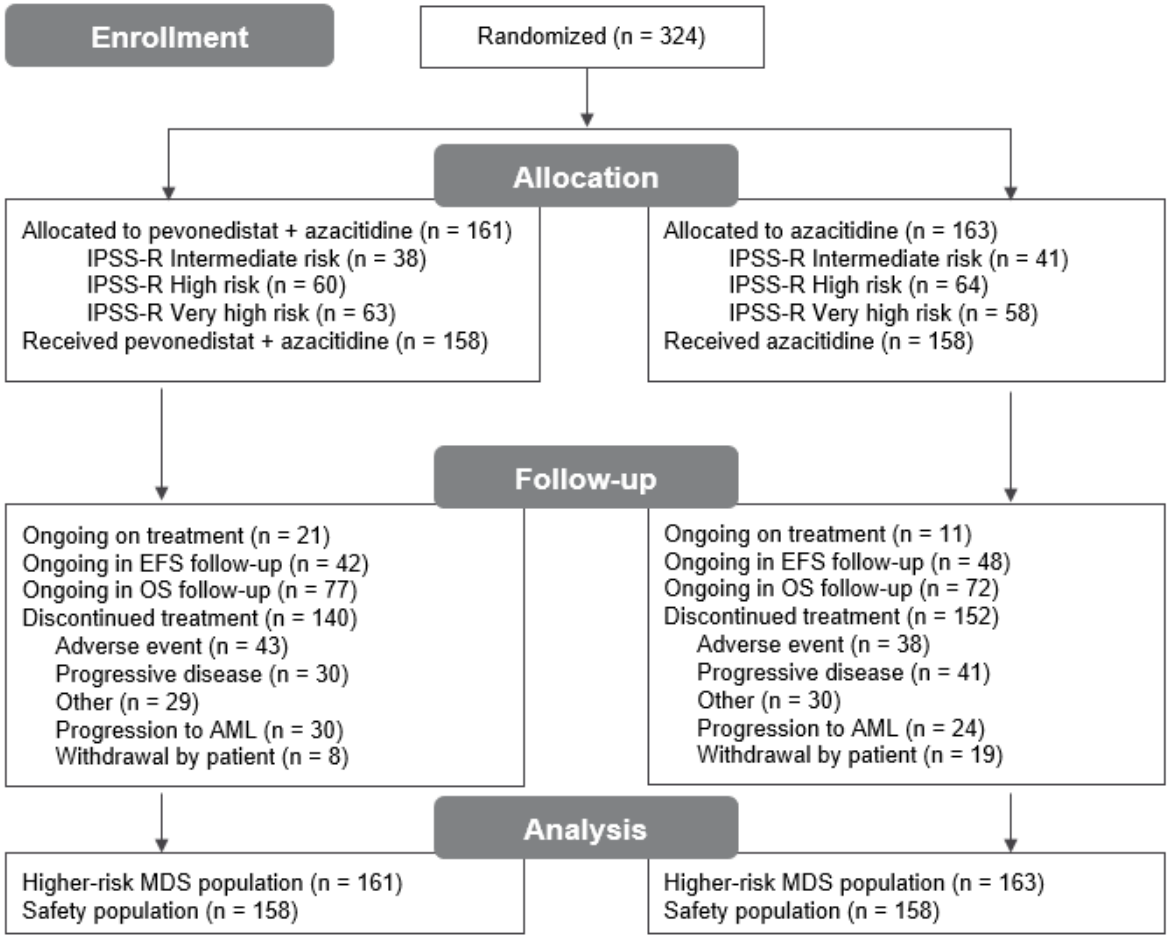


Supplemental Figure 2. CONSORT flow diagrams for the (A) ITT population and (B) higher-risk MDS cohort. AML, acute myeloid leukemia; CMML, chronic myelomonocytic leukemia; EFS, event-free survival; IPSS-R, Revised International Prognostic Scoring System; ITT, intent-to-treat; MDS, myelodysplastic syndromes; OS, overall survival.

A

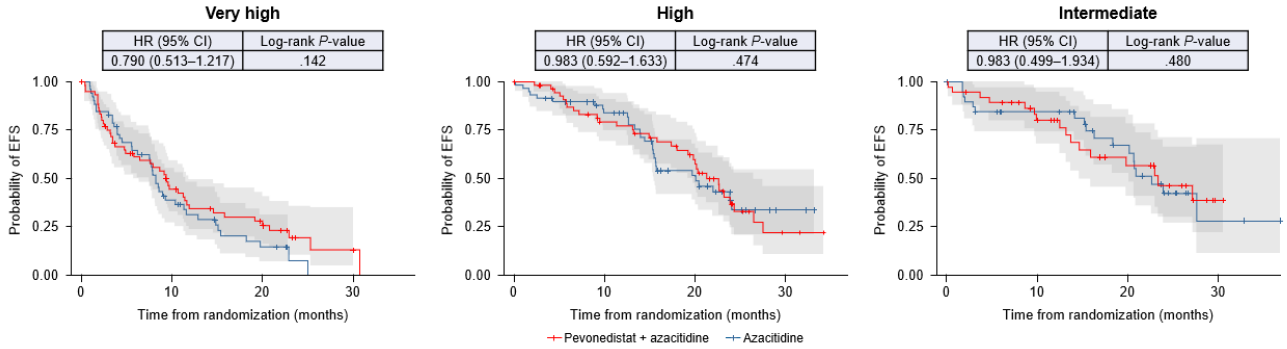


B


Enrollment
Randomized (n = 324)
Allocation
Allocated to pevonedistat + azacitidine (n = 161)
IPSS-R Intermediate risk (n = 38)
IPSS-R High risk (n = 60)
IPSS-R Very high risk (n = 63)
Received pevonedistat + azacitidine (n = 158)
Allocated to azacitidine (n = 163)
IPSS-R Intermediate risk (n = 41)
IPSS-R High risk (n = 64)
IPSS-R Very high risk (n = 58)
Received azacitidine (n = 158)
Follow-up
Ongoing on treatment (n = 21)
Ongoing in EFS follow-up (n = 42)
Ongoing in OS follow-up (n = 77)
Discontinued treatment (n = 140)
Adverse event (n = 43)
Progressive disease (n = 30)
Other (n = 29)
Progression to AML (n = 30)
Withdrawal by patient (n = 8)
Ongoing on treatment (n = 11)
Ongoing in EFS follow-up (n = 48)
Ongoing in OS follow-up (n = 72)
Discontinued treatment (n = 152)
Adverse event (n = 38)
Progressive disease (n = 41)
Other (n = 30)
Progression to AML (n = 24)
Withdrawal by patient (n = 19)
Analysis
Higher-risk MDS population (n = 161)
Safety population (n = 158)
Higher-risk MDS population (n = 163)
Safety population (n = 158)

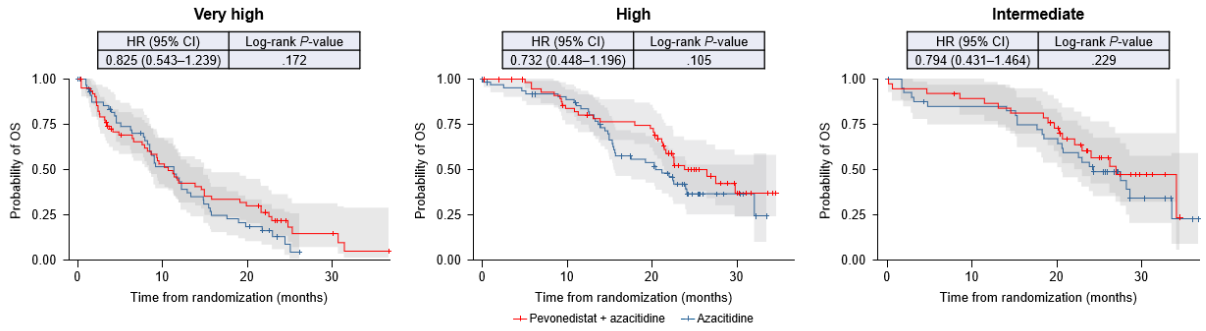
Supplemental Figure 3. Subgroup analysis of (A) EFS and (B) OS by IPSS-R cytogenetic risk subgroups based on IRC assessment in patients with higher-risk MDS. Grey shading represents 95% CI. CI, confidence interval; EFS, event-free survival; IPSS-R, Revised International Prognostic Scoring System; IRC, Independent Review Committee; MDS, myelodysplastic syndromes; OS, overall survival.

A



	Pevonedistat + azacitidine (n=161)	Azacitidine (n=163)	Total (N=324)
IPSS-R category, n (%)			
Very high	63 (39)	58 (36)	121 (37)
High	60 (37)	64 (39)	124 (38)
Intermediate	38 (24)	41 (25)	79 (24)

B



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