A Phase 3, Multicenter, Double-Blind, Randomized, Placebo-Controlled Study of AG-120 in Combination with Azacitidine in Subjects * 18 Years of Age with Previously Untreated Acute Myeloid Leukemia with an IDH1 Mutation

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Primary Objective:* To compare event-free survival (EFS) between AG-120 + azacitidine and placebo + azacitidine. Key Secondary Objectives:* To compare the complete remission (CR) rate between AG-120 + azacitidine and placebo + azacitidine. EFS is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON53147

Source
ToetsingOnline

Brief title
Agios Study for IDH1 Mutation in Acute Myeloid Leukemia (AGILE)

Condition

- Leukaemias

Synonym
Acute Myeloid Leukemia

Research involving

Human

Sponsors and support

Primary sponsor: Institut de Recherches Internationales Servier
Source(s) of monetary or material Support: Agios Pharmaceuticals;Inc.

Intervention

Keyword: AG120, AML, IDH1

Outcome measures

Primary outcome

The primary efficacy endpoint is EFS

Secondary outcome

* CR rate (CR defined as bone marrow blasts < 5% and no Auer rods, absence of extramedullary disease, ANC * 1.0 × 10*9 /L [1000/µL], platelet count * 100 × 10*9 /L [100,000/µL], and independence of RBC transfusions). Sensitivity analyses will be performed to explore the robustness of the primary analysis results and will include an analysis based on the stratified log-rank test following the Intent-to-Treat principle, where the time of relapse or death is determined using the actual date of relapse or death without censoring for missing disease assessments or start of subsequent anticancer therapy.

*OS, defined as the time from date of randomization to the date of death due to any cause.

* CR + CRh rate (CRh is defined as a CR with partial recovery of peripheral blood counts where ANC is >0.5 × 10*9/L [500/*L], and platelet count is >50 × 10*9/L [50,000/µL]; CRh will be derived by the Sponsor)

* ORR, defined as the rate of CR, CRi (including CRp), PR, and MLFS

Study description

Background summary

Acute myeloid leukemia is an aggressive hematologic malignancy with a poor prognosis. Patients not considered candidates for standard IC because of older age with comorbid conditions, poor performance status, or disease-related adverse prognostic risk factors have an especially poor prognosis with a median survival of 2 to 10 months; these patients are commonly treated with BSC or low intensity therapies such as LDAC or hypomethylating agents, including azacitidine. Azacitidine, an analog of the pyrimidine nucleoside cytidine, is a DNA methyltransferase inhibitor that has been shown to be associated with sustained decreases in promoter DNA methylation and altered gene expression at critical regulatory pathways. In addition, azacitidine is a cytotoxic agent. Treatment with azacitidine has demonstrated clinical activity in AML and an encouraging median OS of 9 to 10 months in patients not considered to be eligible for standard IC.

Mutations of the IDH1 enzyme have been identified in several tumors, including AML. The resulting mutant IDH proteins convert alpha ketoglutarate (*-KG) to the oncometabolite 2-HG, which has been shown to cause DNA hypermethylation by inhibition of methylcytosine dioxygenase TET2 and histone hypermethylation through competitive inhibition of * KG dependent Jumonji-C histone demethylases, thereby leading to broad epigenetic changes and a block in myeloid differentiation. AG 120 is a specific inhibitor of IDH1 mutant protein; nonclinical studies have demonstrated that AG-120 effectively inhibits the activity of IDH mutant proteins leading to the reduction of 2-HG in tumors and the reversal of IDH mutation-induced histone and DNA hypermethylation. Preliminary clinical data from the ongoing, open-label, single-agent Phase 1 study in subjects with R/R AML (AG120-C-001) have shown that AG-120 is generally well-tolerated and has triggered the differentiation of leukemic blast cells that ultimately lead to reductions in mean plasma 2-HG concentrations and evidence of substantial clinical activity.

These data raise the possibility that the combination of an inhibitor of the IDH1 mutant protein with a DNA methyltransferase inhibitor such as azacitidine may lead to an additive or synergistic antitumor effect. Azacitidine reduces DNA methylation levels non-specifically, as it inhibits DNA methyltransferase activity, while AG-120 indirectly reduces DNA methylation levels by depleting 2-HG and restoring enzyme function to *-KG-dependent enzymes. A synergistic interaction between azacitidine and AG-120 could have a combined impact on DNA methylation, either at the same DNA loci or potentially at different loci. Furthermore, the combination of AG-120 + azacitidine has been shown to enhance the differentiation and apoptosis of a leukemic cell line (TF-1) that harbors an IDH1 R132 mutation.

Study objective

Primary Objective:
* To compare event-free survival (EFS) between AG-120 + azacitidine and placebo + azacitidine.

Key Secondary Objectives:
* To compare the complete remission (CR) rate between AG-120 + azacitidine and placebo + azacitidine. EFS is defined as the time from randomization until the occurrence of death from any cause, disease relapse after remission or MLFS, progressive disease, or failure to achieve complete remission (CR) or CR with incomplete hematologic (neutrophil and/or platelet) recovery (CRi) (including CR with incomplete platelet recovery [CRp]) at 24 weeks, whichever occurs first, based on responses assessed by the Investigator. Remission is defined as CR or CRi (including CRp). If a subject fails to achieve CR or CRi (including CRp) at 24 weeks, the subject will be considered as an EFS event at that time. EFS will be censored in the event of initiation of a new anticancer therapy should it occur prior to any EFS event.
* To compare overall survival (OS) between AG-120 + azacitidine and placebo + azacitidin. CR is defined as: bone marrow blasts < 5% and no Auer rods; absence of extramedullary disease; absolute neutrophil count (ANC) > 1.0 × 109/L (1000/µL); platelet count > 100 × 109/L (100,000/µL); and independence of red cell transfusions.
* To compare the CR (based on Investigator-assessed IWG Response Criteria for AML) + complete remission with partial hematologic recovery (CRh) rate between AG-120 + azacitidine and placebo + azacitidine. CRh is defined as a CR with partial recovery of peripheral blood counts (< 5% bone marrow blasts, platelets > 50,000/µL, ANC > 500/µL) and will be derived by the Sponsor.
* To compare the objective response rate (ORR) between AG-120 + azacitidine and placebo + azacitidine, as assessed by the Investigator. ORR is defined as the rate of CR, complete remission with incomplete hematologic (neutrophil and/or platelet) recovery (CRi, including complete remission with incomplete platelet recovery [CRp]), partial remission (PR), and morphologic leukemia-free state (MLFS). The best response is calculated using the following hierarchy: 1) CR; 2) CRi (including CRp); 3) PR; and 4) MLFS.

Study design

Study AG120-C-009 is a global, Phase 3, multicenter, double-blind, randomized, placebo-controlled clinical trial to evaluate the efficacy and safety of AG-120 + azacitidine vs placebo + azacitidine in adult subjects with previously untreated IDH1m AML who are considered appropriate candidates for non intensive therapy.

The primary endpoint of OS is defined as the time from date of randomization to the date of death due to any cause. The key secondary efficacy endpoints are

EFS, CR rate, CR + CRh rate (with CRh derived by Sponsor), and ORR.
Following provision of signed informed consent, all subjects will undergo Screening procedures within 4 weeks (28 days) prior to randomization to determine eligibility. Gene mutation analysis for confirmation of IDH1m disease from a bone marrow and/or peripheral blood sample and germ-line mutation analysis from a buccal swab will be conducted for all subjects, and can be conducted prior to the 28-day Screening window. Central laboratory confirmation of IDH1m status is required for study entry. Additional Screening procedures include, but are not limited to: medical and medication history; bone marrow aspirate/biopsy for morphologic analyses and cytogenetics; complete physical examination; vital signs; 12 lead electrocardiogram (ECG); Eastern Cooperative Oncology Group (ECOG) performance status (PS); echocardiogram (ECHO) or multi-gated acquisition (MUGA; not permitted for subjects in Germany) scan for left ventricular ejection fraction (LVEF); clinical laboratory assessments (hematology, chemistry, coagulation, and serum pregnancy test); quality of life (QoL) assessments; and exploratory biomarker assessments.

Subjects eligible for study treatment based on Screening assessments will be randomized 1:1 to receive oral AG-120 or matched placebo, both administered in combination with subcutaneous (SC) or intravenous (IV) azacitidine.
Randomization will be stratified by de novo status (de novo AML and secondary AML) and geographic region (United States/Canada; Western Europe, Israel, and Australia; and rest of world [ROW]).
Subjects should be treated for a minimum of 6 cycles of combination therapy unless they experience relapse after achieving a CR, CRi (including CRp), or MLFS; disease progression after having previously attained PR or stable disease; unacceptable toxicity (adverse event); confirmed pregnancy; withdrawal by subject; physician*s decision to end treatment; protocol violation; death; or End of Study.

Treatment will be administered as follows:
* All subjects will receive azacitidine 75 mg/m2/day SC or IV for the first 1 week (7 days) (or on a 5 2-2 schedule) of each 4-week (28-day) cycle in combination with AG 120 or placebo once daily (QD) on each day of the 4-week cycle. The same schedule should be used for each subject throughout the duration of treatment, when possible.
* Subjects should continue to receive therapy with AG 120 or placebo + azacitidine until death, disease relapse, disease progression, development of unacceptable toxicity (adverse event), confirmed pregnancy, withdrawal by subject, physician*s decision to end treatment, protocol violation, or End of Study.
o Disease progression (defined only for subjects who have previously attained PR or stable disease) is defined as evidence for an increase in bone marrow blast percentage and/or increase of absolute blast counts in the blood: 1) > 50% increase in bone marrow blast count over baseline (a minimum 15% point increase is required in cases with < 30% blasts at baseline); or persistent marrow blast percentage of > 70% over at least 3 months; without at least a

100% improvement in ANC to an absolute level (> 500/µL, and/or platelet count to > 50,000/µL non-transfused); 2)> 50% increase in peripheral blasts (WBC × % blasts) to > 25,000/µL in the absence of treatment-related differentiation syndrome; or 3) new extramedullary disease. All bone marrow blasts, peripheral blood blasts, and extramedullary disease assessments should be confirmed by 2 consecutive assessments separated by at least 4 weeks.
o Subjects with a response less than CR or CRi (including CRp) at 24 weeks or beyond can continue on treatment if demonstrating treatment benefit, defined as any 1 of the following: 1) Transfusion-independence while on study treatment; 2) ANC > 500/µL; or 3) platelets > 50,000/µL.

All subjects will have the extent of their disease assessed by bone marrow aspirate (and biopsy if standard of care) and peripheral blood samples at Screening and Day 1 (± 7 days) of Week 9 and every eighth week thereafter (Weeks 17, 25, etc.); at End of Treatment (EOT); every eighth week during EFS follow-up; as clinically indicated; and/or any time that disease progression is suspected. The disease assessment schedule should not be altered due to changes in the start of treatment cycles (eg, in the case of a treatment interruption that resulted in a delay to the start of subsequent cycles).

During treatment, response will be evaluated by the Investigator based on modified IWG Response Criteria for AML and European LeukemiaNet (ELN) guidelines to determine subject status and continuation on study treatment. Investigator response assessments will be used for the analysis of all efficacy endpoints, unless otherwise defined.

All subjects will undergo safety assessments throughout the treatment period, to include physical examination, vital signs, ECOG PS, ECG, ECHO or MUGA for LVEF as clinically indicated (method per institutional standard of care, with the same method used for an individual subject throughout the study; sites in Germany may only use ECHO), clinical laboratory assessments (hematology, chemistry, and coagulation), and assessment of adverse events (AEs), AEs of special interest (AESIs), serious AEs (SAEs), AEs leading to discontinuation or death, and concomitant medication use. Toxicity severity will be graded according to the National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) version 4.03.

Safety data will be reviewed regularly by an Independent Data Monitoring Committee (IDMC) to ensure the safety of the combination therapy. These reviews will occur after the first 6, 12, 24, and 36 subjects have completed 1 cycle of therapy or discontinued, whichever should occur first. Thereafter, safety reviews will be conducted approximately every 6 months until the study is unblinded for the final efficacy analysis.
There are 2 planned interim analyses for OS. The first is a futility analysis that will be performed when approximately 93 OS events have occurred (approximately 26 months after the first subject is randomized). Consideration to terminate the study will be based on evaluation by the IDMC of the overall

safety and efficacy data available at that time, including an observed hazard ratio (HR) of OS > 1.05 (in favor of the placebo + azacitidine arm), based on the gamma (*2) error spending function. The second interim analysis, for superiority, will be performed when approximately 185 OS events have occurred (approximately 39 months after the first subject is randomized). At this interim analysis, the study could be stopped for efficacy reasons if the observed HR of OS is * 0.691 (1 sided p value * 0.006) in favor of the AG-120 + azacitidine arm, based on the O*Brien-Fleming alpha spending function using the Lan-DeMets method. The overall enrollment period is expected to be approximately 44 months and the study duration is expected to be approximately 54 months. The final analysis of OS will take place when 278 OS events have occurred (approximately 54 months after the first subject is randomized).

All subjects are to undergo an EOT assessment within 1 week of their last dose of study treatment (AG 120/placebo + azacitidine). If a subject discontinues study treatment at a regularly scheduled visit, EOT assessments may be performed at that visit. A post-treatment safety assessment is to be scheduled 4 weeks (± 3 days) after the last dose of study treatment. All subjects who discontinue study treatment without experiencing any one of the following* death, disease relapse, disease progression, failure to achieve CR or CRi (including CRp) at 24 weeks, withdrawal of consent, or start of subsequent anticancer therapy*will be followed every 8 weeks for EFS until the occurrence of 278 OS events.
All subjects who are alive after an EFS event will be contacted every 8 weeks for survival follow-up until death, withdrawal by subject, subject completed study, physician*s decision to end treatment, or loss to follow-up, or until 278 OS events have occurred.

Intervention

AG-120 (500 mg) or matched placebo will be administered orally QD (approximately every 24 hours) during Weeks 1 to 4 in continuous 4 week (28 day) cycles. Subjects may take AG-120 or placebo tablets with or without food. Subjects should be advised that if AG-120/placebo tablets are taken with food, they should avoid consuming a high-fat meal. All subjects will also be advised to avoid grapefruit and grapefruit products.
Azacitidine will be administered SC or IV at a dose of 75 mg/m2/day for 1 week every 4 weeks until the end of the study (unless they are discontinued from treatment), starting on Day 1 (± 3 days). In the event that 2 or fewer doses are missed during the 7 day dosing period, dosing should continue so that the subject receives the full 7 days of therapy. If 3 or more doses are missed during the 7 day dosing period, the Investigator should contact the Medical Monitor and a decision on dosing will be made on an individual case basis. A full 7 days of azacitidine are required, but as per institutional practice, a schedule of 5 days of daily dosing, followed by no dose received on the weekend and 2 daily doses given again at the start of the next week, is allowed. The same schedule should be used for each subject throughout the duration of

treatment, when possible.
On days when both AG-120/placebo and azacitidine are given, AG 120/placebo will be given prior to azacitidine.

Study burden and risks

The required study drug can cause side effects.
- Risks (adverse events) related to Vidaza (Azacitidine) are described in the SmPC Vidaza.
- Risks (adverse events) related to AG-120 are described in the Investigator Brochure AG-120 section 6.5 Potential risks.

Blood Drawing Risks
During this study, small amounts of blood will be drawn from a vein to perform tests that allow your doctors to see how you are doing and to measure the amounts of certain substances in your blood. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising and/or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

Bone Marrow Aspirate and/or Biopsy Risks
Risks associated with bone marrow aspirate and/or biopsy include pain, redness, swelling, excessive bleeding, bruising or infection at the needle site. An allergic reaction to the local anesthetic medication used to numb the skin over the biopsy site may occur.
For more information about side effects and risks, ask your study doctor.

Exposure to radiation
Multigated Acquisition (MUGA) scan during the screening assessments involves using radioactive markers. The total amount of radiation you will be exposed to in this study is 10 mSv. To compare: the background radiation in the Netherlands is ~2.5 mSv per year.
If you participate in scientific research involving exposure to radiation more often, you should discuss with the investigator whether participation now would be safe.
The radiation used during the study may lead to damage to your health. However, this risk is small. We nevertheless advise you not to participate in another scientific study involving exposure to radiation in the near future.
Examinations or procedures involving radiation for medical reasons are not a problem.

Benefit
Isocitrate dehydrogenase 1 (IDH1) is a type of protein involved in normal cell metabolism, the process of providing your body*s cells with energy. In certain types of diseases such as AML, an abnormal form of the IDH1 protein is present in the cancer cells. When IDH1 is present in this form, it produces too much 2-hydroxyglutarate (2-HG), which is a substance that is present in low levels

in normal cells. When too much 2-HG is present, it may prevent immature cells from becoming normal functioning cells, which may result in leukemia. AG-120 may block the abnormal IDH1 protein and may reduce 2-HG levels in diseased cells to normal levels.

Cumulatively, as of 16 January 2020, an estimated 2,187 subjects/patients have been exposed to 1 or more doses of ivosidenib (AG-120), with most subjects/patients exposed in clinical studies and the post-marketed setting. Ivosidenib (AG-120) has been given to approximately 171 healthy volunteers and no serious side effects determined to be related to ivosidenib (AG-120) were noted. In the clinical setting, 897 subjects have received ivosidenib (AG-120), along with 189 subjects who have received ivosidenib in expanded/compassionate use programs, investigator-sponsored studies, and partner studies. Additionally, 1,101 patients received ivosidenib (AG-120) in the post-marketing setting.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

Subjects must meet all of the following criteria to be eligible for inclusion in the study:
1. Be * 18 years of age and meet at least 1 of the following criteria defining ineligibility for intensive induction chemotherapy (IC): a. * 75 years old b. ECOG PS <= 2 c. Severe cardiac disorder (eg, congestive heart failure requiring treatment, LVEF *50%, or chronic stable angina) d. Severe pulmonary disorder (eg, diffusing capacity of the lungs for carbon monoxide *65% or forced expiratory volume in 1 second *65%) e. Creatinine clearance <45 mL/minute f. Bilirubin >1.5 times upper limit of normal (× ULN) g. Any other comorbidity that the Investigator judges to be incompatible with intensive IC must be reviewed and approved by the Medical Monitor before study enrollment. 2. Have previously untreated AML, defined according to World Health Organization (WHO) criteria, with * 20% leukemic blasts in the bone marrow. Subjects with extramedullary disease alone (ie, no detectable bone marrow and no detectable peripheral blood AML) are not eligible for the study. , 3. Have an IDH1 mutation resulting in an R132C, R132G, R132H, R132L, or R132S substitution, as determined by central laboratory testing (using an investigational polymerase chain reaction [PCR] assay, Abbott RealTime IDH1) in their bone marrow aspirate (or peripheral blood sample if bone marrow aspirate is not available).
(Note: Local testing for eligibility and randomization is permitted with medical monitor approval; however, results must state an IDH1 mutation resulting in an R132C, R132G, R132H, R132L, or R132S substitution. Bone marrow aspirate [or peripheral blood sample if bone marrow aspirate is not available with Medical Monitor approval] for central testing must have been sent with proof of shipment to the central laboratory prior to randomization.), 4. Have an ECOG PS score of 0 to 2. , 5. Have adequate hepatic function, as evidenced by:
a. Serum total bilirubin * 2 times the upper limit of normal (× ULN), unless considered to be due to Gilbert*s disease or underlying leukemia, where it must be < 3 × ULN
b. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) * 3.0 × ULN, unless considered to be due to underlying leukemia , 6. Have adequate renal function, as evidenced by serum creatinine * 2.0 × ULN or creatinine clearance > 30 mL/min based on the Cockcroft-Gault glomerular filtration rate. , 7. Have agreed to undergo serial blood and bone marrow sampling. , 8. Be able to understand and willing to sign an informed consent form (ICF). , 9. Be willing to complete QoL assessments during study treatment and at the designated time points following treatment discontinuation. , 10. If female with reproductive potential, must have a negative serum pregnancy test prior to the start of study therapy. Female subjects with reproductive potential are defined as sexually mature women who have not undergone a hysterectomy, bilateral oophorectomy, or tubal occlusion

or who have not been naturally postmenopausal for at least 24 consecutive months. Females of reproductive potential, as well as fertile men with female partners of reproductive potential, must agree to use 2 effective forms of contraception (including at least 1 barrier form) from the time of giving informed consent throughout the study and for 90 days (both females and males) following the last dose of study drug(s). Effective forms of contraception are defined as hormonal oral contraceptives, injectables, patches, intrauterine devices, intrauterine hormone-releasing systems, bilateral tubal ligation, condoms with spermicide, or male partner sterilization.

Exclusion criteria

Subjects who meet any of the following criteria will be excluded from the study:
1. Are candidates for intensive induction chemotherapy (IC) for their AML.

2. Have received any prior treatment for AML with the exception of nononcolytic treatments to stabilize disease such as hydroxyurea or leukapheresis. , 3. Have received a hypomethylating agent for myelodysplastic syndrome (MDS). , 4. Subjects who had previously received treatment for an antecedent hematologic disorder, including investigational agents, may not be randomized until a washout period of at least 5 half-lives of the investigational agent has elapsed since the last dose of that agent. , 5. Have received prior treatment with an IDH1 inhibitor. , 6. Have a known hypersensitivity to any of the components of AG-120, matched placebo, or azacitidine.

7. Are female and pregnant or breastfeeding. , 8. Are taking known strong cytochrome P450 (CYP) 3A4 inducers or sensitive CYP3A4 substrate medications with a narrow therapeutic window, unless they can be transferred to other medications within * 5 half-lives prior to dosing. , Exclusion Criterion #9 was removed in Protocol Amendment 5, Version 6.0.
10. Have an active, uncontrolled, systemic fungal, bacterial, or viral infection without improvement despite appropriate antibiotics, antiviral therapy, and/or other treatment. , 11. Have a prior history of malignancy other than MDS or myeloproliferative disorder, unless the subject has been free of the disease for * 1 year prior to the start of study treatment. However, subjects with the following history/concurrent conditions or similar indolent cancer are allowed to participate in the study:
a. Basal or squamous cell carcinoma of the skin
b. Carcinoma in situ of the cervix
c. Carcinoma in situ of the breast
d. Incidental histologic finding of prostate cancer , 12. Have had significant active cardiac disease within 6 months prior to the start of study treatment, including New York Heart Association Class (NYHA) Class III or IV congestive heart failure, myocardial infarction, unstable angina, and/or stroke. , 13.

Have a heart-rate corrected QT interval using Fridericia*s method (QTcF) * 470 msec or any other factor that increases the risk of QT prolongation or arrhythmic events (eg, NYHA Class III or IV congestive heart failure, hypokalemia, family history of long QT interval syndrome). Subjects with prolonged QTcF interval in the setting of bundle branch block may participate in the study. , 14. Have a known infection caused by human immunodeficiency virus or active hepatitis B virus (HBV), or hepatitis C virus that cannot be controlled by treatment. , 15. Have dysphagia, short-gut syndrome, gastroparesis, or any other condition that limits the ingestion or gastrointestinal absorption of orally administered drugs. , 16. Have uncontrolled hypertension (systolic blood pressure [BP] > 180 mmHg or diastolic BP > 100 mmHg). , 17. Have clinical symptoms suggestive of active central nervous system (CNS) leukemia or known CNS leukemia. Evaluation of cerebrospinal fluid during Screening is only required if there is a clinical suspicion of CNS involvement by leukemia during Screening.

18. Have immediate, life-threatening, severe complications of leukemia, such as uncontrolled bleeding, pneumonia with hypoxia or sepsis, and/or disseminated intravascular coagulation. , 19. Have any other medical or psychological condition deemed by the Investigator to be likely to interfere with the subject*s ability to give informed consent or participate in the study. , 20. Are taking medications that are known to prolong the QT interval unless they can be transferred to other medications within *5 half-lives prior to dosing, or unless the medications can be properly monitored during the study. (If equivalent medication is not available, heart rate corrected Qt interval (QTc) will be closely monitored). 21. Subjects with a known medical history of progressive multifocal leukoencephalopathy..

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:	Recruitment stopped
Start date (anticipated):	19-02-2018
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ivosidenib
Generic name:	Ivosidenib
Product type:	Medicine
Brand name:	Vidaza
Generic name:	Azacitidine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-06-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-02-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-03-2018

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	15-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-01-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2022
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
EudraCT	EUCTR2016-004907-30-NL
ClinicalTrials.gov	NCT03173248
CCMO	NL61316.056.17