Trial record **1 of 1** for: Pran-16-52

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An Efficacy and Safety Study Of Pracinostat In Combination With Azacitidine In Adults With Acute Myeloid Leukemia

This study is currently recruiting participants.

See **Contacts and Locations**

Verified July 2017 by Helsinn Healthcare SA

Sponsor:
Helsinn Healthcare SA

ClinicalTrials.gov Identifier:
NCT03151408

First Posted: May 12, 2017
Last Update Posted: November 14, 2017

Collaborator:
Clinipace LTD
Information provided by (Responsible Party):
Helsinn Healthcare SA

Full Text View | Tabular View | No Study Results Posted | Disclaimer
How to Read a Study Record

Purpose

This is a Phase III, multicenter, double-blind, randomized study of pracinostat vs. placebo with azacitidine (AZA) as background therapy in patients ≥ 18 years of age with newly diagnosed acute myeloid leukemia (AML), excluding acute promyelocytic leukemia and cytogenetic low-risk AML, who are unfit to receive intensive remission induction chemotherapy due to age ≥ 75 years or comorbidities. Patients will be randomized in a 1:1 ratio to one of two groups: Group A (experimental group) to receive pracinostat plus AZA and Group B (control group) to receive placebo plus AZA. Randomization will be stratified by cytogenetic risk category (intermediate vs. unfavorable-risk, according to SWOG Cytogenetic Risk Category Definitions) and ECOG performance status (0-1 vs. 2). Treatments will be administered based on 28-day cycles, with pracinostat/placebo administered orally once every other day, 3 times a week for 3 weeks, followed by one week of no treatment and AZA administered for 7 days of each cycle. Study treatment should continue until there is documented disease progression, relapse from complete remission (CR), or non-manageable toxicity. A minimum of 6 cycles may be required to achieve a complete remission. Once permanently discontinued from study treatment, patients will enter the Long-term Follow-up phase of the study and will be followed for assessment of disease progression, if applicable, and survival every 3 months (±1 month) until death. The end of this study is defined when 390 events (deaths) have occurred and the study is unblinded for final overall survival analysis. Patients who are receiving study treatment at the end of the study may have the opportunity to continue to receive the study drugs to which they were randomized to (Post- Study Observation Period), until the Sponsor informs the Investigators of the appropriate course of action based on the study results. The Post-Study Observation Period is defined as the period starting from the end of the study for a maximum of 12 months.

Condition	Intervention	Phase
Acute Myeloid Leukemia	Drug: Pracinostat Drug: Placebos Drug: Azacitidine	Phase 3

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Phase III, Double-Blind, Placebo-Controlled, Multicenter, Randomized Study Of Pracinostat In Combination With Azacitidine In Patients ≥18 Years With Newly Diagnosed Acute Myeloid Leukemia Unfit For Standard Induction Chemotherapy

Resource links provided by NLM:

Genetics Home Reference related topics: core binding factor acute myeloid leukemia
cytogenetically normal acute myeloid leukemia
familial acute myeloid leukemia with mutated CEBPA

MedlinePlus related topics: Acute Myeloid Leukemia Leukemia

Drug Information available for: Azacitidine

Genetic and Rare Diseases Information Center resources: Myeloid Leukemia
Acute Myeloid Leukemia Acute Non Lymphoblastic Leukemia

U.S. FDA Resources

Further study details as provided by Helsinn Healthcare SA:

Primary Outcome Measures:

- Estimate efficacy rate [Time Frame: from randomization until death from any cause, assessed up to 60 months]

  To show superiority in terms of overall survival (OS) of treatment with pracinostat (Group A - experimental group) versus placebo (Group B - control group) in patients treated with AZA as background therapy

Secondary Outcome Measures:

- Morphologic Complete Remission (CR) rate [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  The CR rate is the proportion of patients who achieve a morphologic CR according to the response criteria

- Event Free Survival (EFS) [Time Frame: from randomization until death from any cause, assessed up to 60 months]

  EFS is defined as the time from randomization to the first documented occurrence of disease progression or disease relapse after CR, or patient death from any cause, whichever occurs first

- Duration of Complete Remission [Time Frame: from complete remission until relapse, assessed up to 60 months]

Duration of Complete Remission is the time from the first documented morphologic CR using the response criteria until documented relapse or death. Duration of CR is only defined for patients who achieve a morphologic CR.

Other Outcome Measures:

- Composite Complete Remission (cCR) rate [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  Composite complete remission (cCR) rate is the proportion of patients who achieve either a disease response of CR, CRi or MLFS (i.e., cCR = CR + CRi + MLFS) within the study period, according to the response criteria

- Cytogenetic Complete Remission (CRc) rate [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  The CRc rate is the proportion of patients who achieve a reversion to a normal karyotype at CR within the study period. This endpoint applies only to patients with abnormal cytogenetic at enrollment

- Molecular Complete Remission rate (CRm) [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  The CRm rate is the proportion of patients who achieve a CR with MRD negativity by multicolor flow cytometry. CRm will be evaluated at the first patient's CR and then after further 4 cycles of treatment

- Duration of Composite Complete Remission [Time Frame: from cCR until relapse, assessed up to 60 months]

  Duration of cCR response is the time from first cCR until documented relapse (the definition of relapse from CR will be applied) or death. Duration of cCR is only defined for patients who achieve a cCR

- Duration of Cytogenetic Complete Remission [Time Frame: from cytogenetic complete remission until relapse, assessed up to 60 months]

  Duration of cytogenetic complete remission is the time from first CRc until documented relapse (defined as reappearance of abnormal karyotype or relapse from CR) or death. Duration of CRc is only defined for patients who achieve a CRc

- Transfusion Independence (TI) [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  Transfusion independence rate is defined as the proportion of patients who show eight weeks or over without red blood cell (RBC-TI) and/or platelet (PLT-TI) transfusion during study period

- Quality of Life [Time Frame: from randomization until end of treatment, assessed up to 48 months]

  Computation of the global health status and of selected functional scales and symptom scales from the EORTC QLQ-C30 questionnaire will be performed and their change from baseline over the study period will constitute the endpoints.

Estimated Enrollment:	500
Actual Study Start Date:	June 23, 2017
Estimated Study Completion Date:	May 2021
Estimated Primary Completion Date:	May 2021 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Pracinostat plus AZA 60 mg capsule orally, once a day, 3 times a week for 3 weeks, followed by 1 week of rest of each 28-day cycle. As a background therapy azacitidine (AZA) will be administered at a dose of 75 mg/m2 by SC or IV injection daily for 7 days of each 28-day cycle.	Drug: Pracinostat 60 mg capsule Other Name: SB939 Drug: Azacitidine SC or IV injection Other Name: AZA
Placebo Comparator: Placebo plus AZA 1 capsule orally, once a day, 3 times a week for 3 weeks, followed by 1 week of rest of each 28-day cycle. As a background therapy azacitidine	Drug: Placebos capsule Drug: Azacitidine

(AZA) will be administered at a dose of 75 mg/m2 by SC or IV injection daily for 7 days of each 28-day cycle.	SC or IV injection Other Name: AZA

Eligibility

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Male or female patient ≥ 18 years of age with newly diagnosed, histologically confirmed, AML including de novo, secondary to antecedent hematologic disorders, or treatment-related disease with intermediate or unfavorable-risk cytogenetics
2. Unable to receive intensive chemotherapy regimens at enrollment, based on one of the following:

   I. Age ≥ 75 years, or

   II. Age < 75 years with at least 1 of the following co-morbidities:

   1. An ECOG performance status of 2
   2. Clinically significant cardiovascular disease defined as:

   i. Left ventricular ejection fraction (LVEF) ≤ 50%, measured within 3 months prior to Day 1 confirmed by ECHO/MUGA ii. Congestive heart failure requiring medical therapy iii. Chronic stable angina requiring medical therapy iv. Prior cerebrovascular accident with sequelae c. Clinically significant pulmonary disease defined as: i. Forced expiratory volume in 1 second (FEV1) ≤ 65% of expected ii. Lung diffusing capacity for carbon monoxide (DLCO) ≤ 65% of expected Confirmed by pulmonary tests. d. Diabetes mellitus

with symptomatic end-organ damage (e.g., retinopathy, nephropathy, neuropathy, vasculopathy) e. Autoimmune inflammatory conditions (e.g., rheumatoid arthritis, systemic lupus erythematous, inflammatory bowel disease, or similar) requiring chronic disease modifying therapy (e.g., etanercept, adalimumab, infliximab, rituximab, methotrexate, or similar) f. Class III obesity defined as a Body Mass Index (BMI) > 40 kg/m2 g. Renal impairment defined as serum creatinine > 1.3 mg/dL (> 115 µmol/L) or creatinine clearance <70 ml/min h. Clinically significant cognitive impairment defined as requiring medical therapy and/or assistance with activities of daily living

3. 20% blasts in bone marrow
4. Peripheral white blood cell (WBC) count 30,000/µL For cyto-reduction, hydroxyurea is allowed during screening and up to Cycle 1, Days 1-14, to reduce WBC count to < 30,000 µL prior to Day 1. After Cycle 1, Day 14, hydroxyurea is prohibited.
5. ECOG performance status ≤ 2
6. Adequate organ function as evidenced by the following laboratory findings:
    1. Total bilirubin ≤ 2 × upper limit of normal (ULN) or < 3 x ULN for patients with Gilbert-Meulengracht Syndrome
    2. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 × ULN
7. Serum creatinine ≤ 1.5 × ULN according to institutional standards or creatinine clearance ≥ 50 mL/min
8. QT-interval corrected according to Fridericia's formula (QTcF) ≤ 450 ms on electrocardiogram (ECG) at Screening
9. Male patient who is surgically sterile, or male patient who is willing to agree to remain completely abstinent (refrain from heterosexual intercourse) or who use barrier contraceptive measures and agree to refrain from donating sperm during the entire study treatment period
10. Female patient who is of childbearing potential willing to use adequate contraceptive measures while participating on study, OR willing to completely abstain from heterosexual intercourse during the entire study treatment period
11. Female patient who is of childbearing potential must have a negative serum pregnancy test result within 3 weeks prior to starting study drugs.
12. Willing to provide voluntary written informed consent before performance of any study related procedure not part of normal medical care
13. Willing and able to understand the nature of this study and to comply with the study and follow-up procedures.

Exclusion Criteria:

1. Able to receive intensive induction chemotherapy

2. AML-associated inv(16)/t(16;16)/del(16q), t(15;17) (i.e. promyelocytic leukemia) with/without secondary aberrations; t(8;21) lacking del (9q) or complex karyotypes
3. Presence of an active malignant disease within the last 12 months, with the exception of adequately treated cervical cancer in-situ, non-melanoma skin cancer and superficial bladder tumors (Ta [non-invasive tumor], Tis [carcinoma in situ] and T1 [tumor invades lamina propria]). Other malignancies may be considered after consultation with the Medical Monitor
4. Life-threatening illnesses other than AML, uncontrolled medical conditions or organ system dysfunction that, in the Investigator's opinion, could compromise the patient's safety or put the study outcomes at risk
5. Uncontrolled arrhythmias; any Class 3-4 cardiac diseases as defined by the New York Heart Association (NYHA) functional classification
6. Evidence of AML central nervous system (CNS) involvement
7. Previous chemotherapy for AML except for the following, which are allowed:
    1. Hydroxyurea for cytoreduction
    2. One course of hypomethylating agent therapy (i.e.; up to 7 doses of azacitidine or 3-5 days of decitabine) within 30 days prior to enrollment (Day 1)
8. Use of experimental drugs ≤ 30 days prior to screening
9. Received prior HDAC inhibitor therapy
10. Received prior treatment with a hypomethylating agent, except as allowed in Exclusion Criterion 7.b
11. Known hypersensitivity to any components of pracinostat, azacitidine, or mannitol
12. History of human immunodeficiency virus (HIV) or an active and uncontrolled infection with hepatitis C virus (HCV) or hepatitis B virus (HBV)
13. Gastrointestinal (GI) tract disease that causes an inability to take oral medication, malabsorption syndrome, or a requirement for IV alimentation; prior surgical procedures affecting absorption; or uncontrolled inflammatory GI disease (e.g., Crohn's disease, ulcerative colitis)
14. Any disease(s), psychiatric condition, metabolic dysfunction, or findings from a physical examination or clinical laboratory test result that would cause reasonable suspicion of a disease or condition, that contraindicates the use of pracinostat and/or AZA, that may increase the risk associated with study participation, that may affect the interpretation of the results, or that would make the patient inappropriate for this study

Contacts and Locations

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03151408***

Contacts

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Locations

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Bethesda, Maryland, United States, 20187

United States, New York

Stony Brook University
Stony Brook, New York, United States, 11794

United States, Ohio

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Cleveland, Ohio, United States, 44106

United States, Oklahoma

Oklahoma cancer specialist and research institute
Tulsa, Oklahoma, United States, 74146

United States, Tennessee

University of Tennessee Medical Center
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Hobart, Tasmania, Australia, 7000

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Le Chesnay, France, 78150

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Paris, France, 75475

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Sponsors and Collaborators

Helsinn Healthcare SA

Clinipace LTD

Investigators

Study Chair: Guillermo Garcia-Manero, MD MD Anderson

More Information

Responsible Party: Helsinn Healthcare SA
ClinicalTrials.gov Identifier: NCT03151408 History of Changes

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Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Keywords provided by Helsinn Healthcare SA:
AML

Additional relevant MeSH terms:

Leukemia
Leukemia, Myeloid
Leukemia, Myeloid, Acute
Neoplasms by Histologic Type
Neoplasms
Azacitidine
Antimetabolites, Antineoplastic
Antimetabolites
Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents
Enzyme Inhibitors