Trial record **1 of 1** for: 2215-CL-0201

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A Study of ASP2215 (Gilteritinib) by Itself, ASP2215 Combined With Azacitidine or Azacitidine by Itself to Treat Adult Patients Who Have Recently Been Diagnosed With Acute Myeloid Leukemia With a FLT3 Gene Mutation and Who Cannot Receive Standard Chemotherapy

ClinicalTrials.gov Identifier: NCT02752035

Recruitment Status : Recruiting
First Posted : April 26, 2016
Last Update Posted : December 11, 2017

See **Contacts and Locations**

Sponsor:
Astellas Pharma Global Development, Inc.

Information provided by (Responsible Party):
Astellas Pharma Inc (Astellas Pharma Global Development, Inc.)

Study Details | **Tabular View** | **No Results Posted** | Disclaimer

Study Description

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Brief Summary:

This is a clinical study for adult patients who have recently been diagnosed with acute myeloid leukemia or AML. AML is a type of cancer. It is when bone marrow makes white blood cells that are not normal. These are called leukemia cells. Some patients with AML have a mutation, or change, in the FLT3 gene. This gene helps leukemia cells make a protein called FLT3. This protein causes the leukemia cells to grow faster. For patients with AML who cannot receive standard chemotherapy, azacitidine (also known as Vidaza®) is a current standard of care treatment option in the United States. This clinical study is testing an experimental medicine called ASP2215, also known as gilteritinib. Gilteritinib works by stopping the leukemia cells from making the FLT3 protein. This can help stop the leukemia cells from growing faster. This study will compare three different treatments. Patients are assigned to one of these three groups by chance: an experimental medicine gilteritinib, a different medicine called azacitidine, also known as Vidaza®, or both medicines (azacitidine and gilteritinib) together. The clinical study may help show which treatment helps patients live longer.

Condition or disease	Intervention/treatment	Phase
Acute Myeloid Leukemia (AML) Acute Myeloid Leukemia With FMS-like Tyrosine Kinase (FLT3) Mutation	Drug: gilteritinib Drug: azacitidine	Phase 2 Phase 3

Access to an investigational treatment associated with this study is available outside the clinical trial.

More info ...

Detailed Description:

Subjects considered an adult according to local regulation at the time of obtaining informed consent may participate in the study.

Safety Cohort Prior to initiation of the randomized trial, 8 to 12 subjects will be enrolled to evaluate the safety and tolerability of ASP2215 given with azacitidine therapy in the study population.

Randomized Trial Approximately 528 subjects will be randomized in a 1:1:1 ratio to receive ASP2215 (Arm A), ASP2215 plus azacitidine (Arm AC) or azacitidine only (Arm C).

Subjects will enter the screening period up to 14 days prior to the start of treatment. Subjects will be administered treatment over 28-day cycles.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	540 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase 2/3 Multicenter, Open-label, 3-arm, 2-Stage Randomized Study of ASP2215 (Gilteritinib), Combination of ASP2215 Plus Azacitidine and Azacitidine Alone in the Treatment of Newly Diagnosed Acute Myeloid Leukemia With FLT3 Mutation in Patients Not Eligible for Intensive Induction Chemotherapy
Actual Study Start Date :	August 1, 2016
Estimated Primary Completion Date :	May 2020
Estimated Study Completion Date :	October 2020

Resource links provided by the National Library of Medicine

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

Arms and Interventions

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Arm	Intervention/treatment

Experimental: Dose escalation of ASP2215 given with azacitidine Subjects will be treated with ASP2215 daily (days 1-28) and azacitidine daily for 7 days (days 1-7).	Drug: gilteritinib Tablet, oral Other Name: ASP2215 Drug: azacitidine Subcutaneous injection or intravenous infusion
Experimental: Arm A: ASP2215 Subjects will be treated daily each 28-day cycle.	Drug: gilteritinib Tablet, oral Other Name: ASP2215
Experimental: Arm AC: ASP2215 + azacitidine Subjects will be treated with ASP2215 daily and azacitidine daily for 7 days (days 1-7) each 28-day cycle.	Drug: gilteritinib Tablet, oral Other Name: ASP2215 Drug: azacitidine Subcutaneous injection or intravenous infusion
Active Comparator: Arm C: azacitidine Subjects will be treated with azacitidine for 7 days (days 1-7) each 28-day cycle.	Drug: azacitidine Subcutaneous injection or intravenous infusion

Outcome Measures

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Primary Outcome Measures :

1. Overall survival (OS) [Time Frame: Up to 36 months]

   OS is defined as the time from the date of randomization until the date of death from any cause.

Secondary Outcome Measures :

1. Event free survival (EFS) [Time Frame: Up to 36 months]

   EFS is defined as the time from the date of randomization until the date of documented relapse from complete remission (CR), complete remission with incomplete platelet recovery (CRp) or complete remission with incomplete hematologic recovery (Cri), treatment failure or death from any cause, whichever occurs first.

2. Best response [Time Frame: Up to 36 months]

   Best response is defined as the best measured response (CR, CRp, Cri or treatment failure) posttreatment

3. Leukemia free survival (LFS) [Time Frame: Up to 36 months]

   LFS is defined as the time from the date of first composite complete remission (CRc) until the date of documented relapse or death for subjects who achieve CRc.

4. Duration of remission [Time Frame: Up to 36 months]

   Duration of remission includes duration of CRc, CR, Cri, CRp and response (CRc + partial response [PR]). Duration of CRc is defined as the time from the date of first CRc until the date of documented relapse for subjects who achieve CRc. Duration of remission is similarly defined for CR, Cri and CRp.

5. Participant reported fatigue from Brief Fatigue Inventory (BFI) [Time Frame: Up to 36 months]

   The BFI was developed to assess the severity of fatigue and the impact of fatigue on daily functioning in subjects with fatigue due to cancer and cancer treatment The BFI inventory has 9 items and a 24-hour recall. A global fatigue score is computed by averaging the 9 items.

6. Safety assessed by adverse events (AEs) [Time Frame: Up to 36 months]
7. Number of participants with abnormal laboratory values and/or adverse events related to treatment [Time Frame: Up to 36 months]
8. Number of participants with abnormal vital signs and/or adverse events related to treatment [Time Frame: Up to 36 months]
9. Safety assessed by electrocardiograms (ECGs) [Time Frame: Up to 36 months]

   The 12-lead ECGs will be recorded in triplicate (3 separate ECGs) and transmitted electronically for central reading. The mean of the triplicate ECG from central read will be used for all final treatment decisions and adverse event reporting.

10. Eastern Cooperative Oncology Group (ECOG) performance status score [Time Frame: Up to 36 months]

    ECOG performance status measured on 6 point scale to assess participant's performance status. 0=Fully active, able to carry on all pre-disease activities without restriction; 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; 2= Ambulatory and capable of all self-

care but unable to carry out any work activities. Up and about more than 50% of waking hours; 3=Capable of only limited self-care, confined to bed or chair more than 50% of waking hours; 4=Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair; 5=Dead. 0=Best status; 5=Worst status.

Eligibility Criteria

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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:

- Subject is considered an adult according to local regulation at the time of obtaining informed consent.
- Subject has a diagnosis of previously-untreated AML according to World Health Organization (WHO) classification [Swerdlow et al, 2008] as determined by pathology review at the treating institution.
- Subject is positive for FLT3 mutation (internal tandem duplication [ITD] or tyrosine kinase domain [TKD] [D835/I836] mutation) in bone marrow or whole blood as determined by central laboratory. Note: Only applicable to the randomization portion.
- Subject is ineligible for intensive induction chemotherapy by meeting at least 1 of the following criteria:
    1. Subject is ≥ 75 years of age.
    2. Subject has any of the following comorbidities:

        - Congestive heart failure (New York Heart Association {NYHA} class ≤ 3) or ejection fraction (Ef) ≤ 50%;
        - Creatinine > 2 mg/dL (177 µmol/L), dialysis or prior renal transplant;
        - ECOG performance status ≥ 3;
        - Prior or current malignancy that does not require concurrent treatment;
        - Subject has received a cumulative anthracycline dose above 400 mg/m2 of doxorubicin (or cumulative maximum dose of another anthracycline).
- Subject must meet the following criteria as indicated on the clinical laboratory tests:
    - Serum AST and ALT ≤ 2.5 x Institutional upper limit of normal (ULN)
    - Serum total bilirubin ≤ 1.5 x Institutional ULN
    - Serum potassium ≥ Institutional lower limit of normal (LLN)
    - Serum magnesium ≥ Institutional LLN
- Subject is suitable for oral administration of study drug.
- Female subject must either:
    - Be of nonchildbearing potential:
        - Postmenopausal (defined as at least 1 year without any menses) prior to screening, or
        - Documented surgically sterile or status posthysterectomy (at least 1 month prior to screening)
    - Or, if of childbearing potential,
        - Agree not to try to become pregnant during the study and for 180 days after the final study drug administration
        - And have a negative urine or serum pregnancy test at screening
        - And, if heterosexually active, agree to consistently use 2 forms of effective contraception per locally accepted standards, 1 of which must be a barrier method, starting at screening and throughout the study period and for 180 days after the final study drug administration.
- Female subject must agree not to breastfeed starting at screening and throughout the study period, and for 60 days after the final study drug administration.
- Female subject must not donate ova starting at screening and throughout the study period, and for 180 days after the final study drug administration.
- Male subject and their female partners who are of childbearing potential must be using 2 forms of effective contraception per locally accepted standards, 1 of which must be a

barrier method, starting at screening and continue throughout the study period, and for 120 days after the final study drug administration.

- Male subject must not donate sperm starting at screening and throughout the study period and for 120 days after the final study drug administration.
- Subject agrees not to participate in another interventional study while on treatment.

Exclusion Criteria:

- Subject was diagnosed as acute promyelocytic leukemia (APL).
- Subject has BCR-ABL-positive leukemia (chronic myelogenous leukemia in blast crisis).
- Subject has received previous therapy for AML, with the exception of the following:
  - Emergency leukapheresis
  - Hydroxyurea for ≤ 14 days
  - Preemptive treatment with retinoic acid prior to exclusion of APL ≤ 7 days
  - Growth factor or cytokine support
  - Steroids for the treatment of hypersensitivity or transfusion reactions, nausea/vomiting or pain
- Subject has clinically active central nervous system leukemia.
- Subject has been diagnosed with another malignancy that requires concurrent treatment or hepatic malignancy regardless of need for treatment.
- Subject has clinically significant coagulation abnormality unless secondary to AML.
- Subject has had major surgery within 4 weeks prior to the first study dose.
- Subject has radiation therapy within 4 weeks prior to the first study dose.
- Subject requires treatment with concomitant drugs that are strong inducers of cytochrome P450 CYP3A.
- Subject requires treatment with concomitant drugs that are strong inhibitors or inducers of P-gp with the exception of drugs that are considered absolutely essential for the care of the subject.
- Subject requires treatment with concomitant drugs that target serotonin 5HT1R or 5HT2BR or sigma nonspecific receptor with the exception of drugs that are considered absolutely essential for the care of the subject.
- Subject has congestive heart failure classified as New York Heart Association Class IV.
- Subject with mean Fridericia-corrected QT interval (QTcF) > 450 ms at screening based on central reading.
- Subject with a history of Long QT Syndrome at screening.
- Subject has known pulmonary disease with diffusion capacity of lung for carbon monoxide (DLCO) ≤ 65%, forced expiratory volume in the first second (FEV1) ≤ 65%, dyspnea at rest

or requiring oxygen or any pleural neoplasm (Transient use of supplemental oxygen is allowed.)

- Subject has an active uncontrolled infection. If an infection is present, the patient must be receiving definitive therapy and have no signs of progressing infection. Progressing infection is defined as hemodynamic instability attributable to sepsis or new symptoms, worsening physical signs or radiographic findings attributable to infection. Persisting fever without other signs or symptoms will not be interpreted as progressing infection.
- Subject is known to have human immunodeficiency virus infection.
- Subject has active hepatitis B or C or other active hepatic disorder.
- Subject has any condition which makes the subject unsuitable for study participation, including any contraindications of azacitidine.

Contacts and Locations

Go to

Information from the National Library of Medicine NIH NLM

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): ***NCT02752035***

Contacts

Contact: Astellas Pharma Global Development 800-888-7704 ext 5473 astellas.registration@

Show 123 Study Locations

Sponsors and Collaborators

Astellas Pharma Global Development, Inc.

Investigators

Study Director: Medical Director Astellas Pharma Global Development, Inc.

More Information

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Responsible Party:	Astellas Pharma Global Development, Inc.
ClinicalTrials.gov Identifier:	NCT02752035 History of Changes
Other Study ID Numbers:	**2215-CL-0201**
	2015-001790-41 (EudraCT Number)
First Posted:	April 26, 2016 Key Record Dates
Last Update Posted:	December 11, 2017
Last Verified:	December 2017

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Keywords provided by Astellas Pharma Inc (Astellas Pharma Global Development, Inc.):

AML
ASP2215
Newly Diagnosed AML
gilteritinib
Acute Myeloid Leukemia (AML)
FLT3

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