An Open-label Study of Quizartinib Monotherapy vs. Salvage Chemotherapy in Acute Myeloid Leukemia (AML) Subjects

This study is currently recruiting participants. (see Contacts and Locations)

Verified December 2015 by *Daiichi Sankyo Inc.*

Sponsor:
Daiichi Sankyo Inc.

Information provided by (Responsible Party):
Daiichi Sankyo Inc.

ClinicalTrials.gov Identifier:
NCT02039726

First received: January 15, 2014
Last updated: December 23, 2015
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History of Changes

Purpose

The primary objective of the study is to determine w hether quizartinib monotherapy prolongs overall survival (OS) compared to salvage chemotherapy in subjects w ith FMS-like tyrosine kinase 3 - Internal Tandem Duplication (FLT3-ITD) positive AML w ho are refractory to or have relapsed w ithin 6 months, after first-line AML therapy.

Condition	Intervention	Phase
AML	Drug: Quizartinib Drug: Salvage Chemotherapy	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase 3 Open-label Randomized Study of Quizartinib (AC220) Monotherapy Versus Salvage Chemotherapy in Subjects With Tyrosine Kinase 3 - Internal Tandem Duplication (FLT3-ITD) Positive Acute Myeloid Leukemia (AML) Refractory to or Relapsed After First-line Treatment With or Without Hematopoietic Stem Cell Transplantation (HSCT) Consolidation

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 w ith mutated CEBPA

MedlinePlus related topics: Acute Myeloid Leukemia Leukemia

Drug Information available for: Cytarabine Mitoxantrone Lenograstim Granulocyte colony-stimulating factor

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

U.S. FDA Resources

Further study details as provided by Daiichi Sankyo Inc.:

Primary Outcome Measures:

- Overall Survival [Time Frame: 2 years] [Designated as safety issue: Yes]

  The primary objective of the study is to determine w hether quizartinib monotherapy prolongs overall survival (OS) compared to salvage

chemotherapy in subjects with FMS-like tyrosine kinase 3 (FLT3-ITD) positive Acute Myeloid Leukemia (AML) who are refractory to or have relapsed within 6 months, after first-line Acute Myeloid Leukemia (AML) therapy.

Secondary Outcome Measures:

- Event-Free Survival [Time Frame: 2 years] [Designated as safety issue: Yes]

  The secondary objective is to determine event-free survival (EFS) with quizartinib versus salvage chemotherapy.

Estimated Enrollment:	326
Study Start Date:	April 2014
Estimated Study Completion Date:	July 2017
Estimated Primary Completion Date:	May 2017 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Quizartinib 20 or 30 mg quizartinib tablets	Drug: Quizartinib no details to specify Other Name: AC220
Active Comparator: Salvage chemotherapy Low dose cytarabine (LoDAC); mitoxantrone, etoposide, and intermediate-dose cytarabine (MEC); or fludarabine, cytarabine, and granulocyte colony stimulating factor (G-CSF) with idarubicin (FLAG-IDA)	Drug: Salvage Chemotherapy No details to specify. Other Name: Low dose cytarabine; mitoxantrone, etoposide and intermediate-dose cytarabine; cytarabine and granulocyte colony stimulating factor with idarubicin

Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Provision of written informed consent approved by the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) with privacy language in accordance with national regulations (e.g., Health Insurance Portability and Accountability Act (HIPAA)) authorization for United States (US) sites prior to any study related procedures, including withdrawal of prohibited medications if applicable.
2. Age ≥18 years at the time of informed consent.
3. Morphologically documented primary Acute Myeloid Leukemia (AML) or AML secondary to Myelodysplastic Syndrome (MDS), as defined by World Health Organization (WHO) criteria, as determined by pathology review at the study site.
4. In first relapse (with duration of remission of 6 months or less) or refractory after prior therapy, with or without HSCT. Induction therapy must have included at least 1 cycle of an anthracycline/mitoxantrone-containing induction block at a standard dose.
5. Presence of the FLT3-ITD activating mutation in bone marrow or peripheral blood (allelic ratio as determined by a central laboratory with a cutoff of ≥3% FLT3 ITD/total FLT3).
6. Eligibility for pre-selected salvage chemotherapy, according to the Investigator's assessment.
7. Eastern Cooperative Oncology Group (ECOG) performance score 0-2.
8. Discontinuation of prior AML treatment before the start of study treatment (except hydroxyurea or other treatment to control leukocytosis) for at least 2 weeks for cytotoxic agents, or for at least 5 half-lives for non cytotoxic agents.
9. Serum creatinine ≤1.5×upper limit of normal (ULN), or glomerular filtration rate >25 mL/min, as calculated with the Cockcroft-Gault formula.
10. Serum potassium, magnesium, and calcium (serum calcium corrected for hypoalbuminemia) within institutional normal limits. Subjects with electrolytes outside the normal range will be eligible if these values are corrected upon retesting following any necessary supplementation.
11. Total serum bilirubin ≤1.5×ULN.
12. Serum aspartate transaminase (AST) and/or alanine transaminase (ALT) ≤2.5×ULN.

Exclusion Criteria:

1. Acute Promyelocytic Leukemia (AML subtype M3).

2. AML secondary to prior chemotherapy for other neoplasms, except AML secondary to prior Myelodysplastic Syndrome (MDS).
3. History of another malignancy, unless the candidate has been disease-free for at least 5 years.
4. Persistent, clinically significant > Grade 1 non-hematologic toxicity from prior AML therapy.
5. Clinically significant graft versus host disease (GVHD) or GVHD requiring initiation of treatment or treatment escalation within 21 days, and/or > Grade 1 persistent or clinically significant non hematologic toxicity related to HSCT.
6. History of or current, central nervous system involvement with AML.
7. Clinically significant coagulation abnormality, such as disseminated intravascular coagulation.
8. Prior treatment with a FLT3 targeted therapy including sorafenib or investigational FLT3 inhibitors.
9. Known presence of a FLT3-D835 mutation at study enrollment. For a candidate who has received prior FLT3-targeted therapy (with the exception of midostaurin), the absence of a baseline FLT3-D835 mutation at study enrollment must be documented.
10. Major surgery within 4 weeks prior to screening.
11. Radiation therapy within 4 weeks prior to screening.
12. Uncontrolled or significant cardiovascular disease
13. Active infection not well controlled by antibacterial or antiviral therapy.
14. Known infection with human immunodeficiency virus, or active hepatitis B or C, or other active clinically relevant liver disease.
15. Unwillingness to receive infusion of blood products according to the protocol.
16. In a man whose sexual partner is a woman of childbearing potential, unwillingness or inability of the man or woman to use an acceptable contraceptive method for the entire study treatment period and for at least 3 months after study treatment completion. Male subjects must not donate sperm starting at Screening and throughout the study period, and 105 days after the final study drug administration.
17. In a woman of childbearing potential, unwillingness or inability to use an acceptable contraceptive method for the entire study treatment period and for at least 3 months after study treatment completion. Additionally, for women randomized to chemotherapy, unwillingness to adhere to the restrictions in the respective Summary of Product Characteristics and the Patient Information Leaflet (package insert) as instructed by the Investigator. Female subjects must not donate ova started at Screening and throughout the study treatment period, and for 105 days after the final study drug administration.
18. Pregnancy.
19. Female subjects must agree not to breastfeed at Screening and throughout the study period, and for 45 days after the final study drug administration.
20. Medical condition, serious intercurrent illness, or other circumstance that, in the Investigator's judgment, could jeopardize the candidate's safety as a study subject, or that could interfere with study objectives.

For subjects in the UK only: Refusal of permission to allow the subject's General Practitioner to be notified of their participation in the study.

Contacts and Locations

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, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02039726

Contacts

Contact: Guy Gammon, MBBS 858-334-2165 ggammon@dsi.com

Contact: Melissa Holmes 858-334-4829 mholmes@dsi.com

Show 113 Study Locations

Sponsors and Collaborators

Daiichi Sankyo Inc.

Investigators

Principal Investigator: Jorge E. Cortes, MD MD Anderson

More Information

No publications provided

Responsible Party: Daiichi Sankyo Inc.
ClinicalTrials.gov Identifier: NCT02039726 History of Changes

Other Study ID Numbers:	**AC220-007**, EudraCT Number 2013-004890-28
Study First Received:	January 15, 2014
Last Updated:	December 23, 2015
Health Authority:	United States: Food and Drug Administration Australia: Department of Health and Ageing Therapeutic Goods Administration

Keywords provided by Daiichi Sankyo Inc.:

Acute Myeloid Leukemia
AML
FMS-like tyrosine kinase 3
FLT3-ITD
Quizartinib
Leukemia
Tablets

Additional relevant MeSH terms:

Leukemia, Myeloid
Leukemia, Myeloid, Acute
Leukemia
Neoplasms
Neoplasms by Histologic Type
Cytarabine
Lenograstim
Mitoxantrone
Adjuvants, Immunologic
Analgesics
Anti-Infective Agents
Antimetabolites
Antimetabolites, Antineoplastic
Antineoplastic Agents
Antiviral Agents
Central Nervous System Agents
Enzyme Inhibitors
Immunologic Factors
Immunosuppressive Agents
Molecular Mechanisms of Pharmacological Action
Peripheral Nervous System Agents
Pharmacologic Actions
Physiological Effects of Drugs
Sensory System Agents
Therapeutic Uses
Topoisomerase II Inhibitors
Topoisomerase Inhibitors