Ponatinib in Patients With Resistant Chronic Phase Chronic Myeloid Leukemia (CML) to Characterize the Efficacy and Safety of a Range of Doses (OPTIC)

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

Verified November 2015 by Ariad Pharmaceuticals

Sponsor:
Ariad Pharmaceuticals

Information provided by (Responsible Party):
Ariad Pharmaceuticals

ClinicalTrials.gov Identifier:
NCT02467270

First received: June 2, 2015
Last updated: November 7, 2016
Last verified: November 2015
History of Changes

Purpose

The purpose of this study is to compare and characterize the efficacy and safety of ponatinib in patients with resistant chronic myeloid leukemia (CML) in chronic phase (CP) in a range of doses.

Condition	Intervention	Phase
Myeloid Leukemia, Chronic, Chronic Phase	Drug: ponatinib 45 mg Drug: ponatinib 30 mg Drug: ponatinib 15 mg	Phase 2

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 Randomized, Open-label, Phase 2 Trial of Ponatinib in Patients With Resistant Chronic Phase Chronic Myeloid Leukemia to Characterize the Efficacy and Safety of a Range of Doses

Resource links provided by NLM:

Genetics Home Reference related topics: chronic myeloid leukemia

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Ponatinib Ponatinib hydrochloride

Genetic and Rare Diseases Information Center resources: Myeloid Leukemia Chronic Myeloid Leukemia Chronic Myeloproliferative Disorders

U.S. FDA Resources

Further study details as provided by Ariad Pharmaceuticals:

Primary Outcome Measures:

- Major cytogenetic response (MCyR) [Time Frame: 12 months] [Designated as safety issue: No]

  MCyR is the presence of 0-35% of Ph+ cells in bone marrow. Response is further defined as partial cytogenetic response (PCyR), complete cytogenetic response (CCyR), or ≤1% BCR ABL(IS) (i.e., MR2), which is equivalent to CCyR.

Secondary Outcome Measures:

- Rates of vascular occlusive events (VOEs), adverse events (AEs), and serious AEs (SAEs) [Time Frame: 24 months]
  [Designated as safety issue: Yes]

  VOEs will be categorized as arterial or venous and according to main vasculature affected (cardiovascular, cerebrovascular or peripheral vascular).

- Safety measured by comparing frequencies of AEs, SAEs and VOEs [Time Frame: 24 months] [Designated as safety issue: Yes]
- Analysis of the relationship between steady-state plasma ponatinib exposure [peak plasma concentration (CMAX) and area-under-the-curve (AUC)] and safety measures (VOEs and any AEs that occur in at least 30 patients) [Time Frame: 24 months]
  [Designated as safety issue: Yes]
- Analysis of the relationship between steady-state plasma ponatinib exposure (AUC and CMAX) and efficacy measures (MCyR, MR2, and MMR) [Time Frame: 24 months] [Designated as safety issue: No]

Estimated Enrollment:	450
Study Start Date:	June 2015
Estimated Study Completion Date:	December 2018
Estimated Primary Completion Date:	December 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Cohort A ponatinib 45 mg once daily starting dose	Drug: ponatinib 45 mg 45 mg tablet, taken orally once daily Other Names: • Iclusig • AP24534
Experimental: Cohort B ponatinib 30 mg once daily starting dose	Drug: ponatinib 30 mg 30 mg tablet, taken orally once daily Other Names: • Iclusig • AP24534
Experimental: Cohort C ponatinib 15 mg once daily starting dose	Drug: ponatinib 15 mg 15 mg tablet, taken orally once daily Other Names: • Iclusig • AP24534

Detailed Description:
This is a multi-center, randomized, phase 2 trial to characterize the safety and efficacy of ponatinib over a range of 3 starting doses. Eligible patients must have chronic phase chronic myeloid leukemia (CP-CML) and be resistant to at least 2 tyrosine kinase inhibitors (TKIs).

Eligibility

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

Criteria

Inclusion Criteria:

1. Have CP-CML and are resistant to at least two prior TKIs
2. Be male or female patients ≥18 years old
3. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
4. Have adequate renal function as defined by the following criterion:
   - Serum creatinine ≤1.5 × upper limit of normal (ULN) for institution
5. Have adequate hepatic function as defined by the following criteria:
   - Total serum bilirubin ≤1.5 × ULN, unless due to Gilbert's syndrome
   - Alanine transaminase (ALT) ≤2.5 × ULN, or ≤5 × ULN if leukemic involvement of the liver is present
   - Aspartate transaminase (AST) ≤2.5 × ULN, or ≤5 × ULN if leukemic involvement of the liver is present

Exclusion Criteria:

1. Have used any approved TKIs or investigational agents within 2 weeks or 6 half-lives of the agent, whichever is longer, prior to receiving study drug

2. Received interferon, cytarabine, or immunotherapy within 14 days, or any other cytotoxic chemotherapy, radiotherapy, or investigational therapy within 28 days prior to receiving the first dose of ponatinib, or have not recovered (> grade 1 by NCI Common Toxicity Criteria for Adverse Effects (CTCAE), version 4.0) from AEs (except alopecia), due to agents previously administered
3. Have undergone autologous or allogeneic stem cell transplant <60 days prior to receiving the first dose of ponatinib; have any evidence of ongoing graft-versus-host disease (GVHD) or GVHD requiring immunosuppressive therapy or are being considered for stem cell transplant within 6-12 months of enrollment (note: ponatinib is not to be used as a bridge to stem cell transplant in this trial)
4. Are taking medications with a known risk of Torsades de Pointes
5. Have clinically significant, uncontrolled, or active cardiovascular disease, specifically including, but not restricted to:
    - Any history of myocardial infarction (MI), unstable angina, cerebrovascular accident, or Transient Ischemic Attack (TIA)
    - Any history of peripheral vascular infarction, including visceral infarction
    - Any revascularization procedure, including the placement of a stent
    - Congestive heart failure (NYHA class III or IV) within 6 months prior to enrollment, or left ventricular ejection fraction (LVEF) less than lower limit of normal, per local institutional standards, within 6 months prior to enrollment
    - History of clinically significant (as determined by the treating physician) atrial arrhythmia or any history of ventricular arrhythmia
    - Venous thromboembolism, including deep venous thrombosis or pulmonary embolism, within 6 months prior to enrollment

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: NCT02467270

Contacts

Contact: Heinrich Farin, MD (617) 494-0400 Heinrich.Farin@ARIAD.com

Show 92 Study Locations

Sponsors and Collaborators

Ariad Pharmaceuticals

More Information

Additional Information:

Iclusig® (ponatinib) US Prescribing Information EXIT

Responsible Party:	Ariad Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT02467270 History of Changes
Other Study ID Numbers:	**AP24534-14-203** 2014-001617-12
Study First Received:	June 2, 2015
Last Updated:	November 7, 2016
Health Authority:	United States: Food and Drug Administration Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Australia: Department of Health and Ageing Therapeutic Goods Administration Belgium: Federal Agency for Medicines and Health Products, FAMHP Canada: Health Canada Chile: Instituto de Salud Pública de Chile Czech Republic: State Institute for Drug Control Denmark: Danish Health and Medicines Authority Finland: Finnish Medicines Agency France: Agence Nationale de Sécurité du Médicament et des produits de santé Germany: Federal Institute for Drugs and Medical Devices Hong Kong: Department of Health Italy: The Italian Medicines Agency Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) Norway: Norwegian Medicines Agency Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Singapore: Health Sciences Authority Korea: Ministry of Food and Drug Safety Spain: Agencia Española de Medicamentos y Productos Sanitarios Sweden: Medical Products Agency Switzerland: Swissmedic Taiwan : Food and Drug Administration United Kingdom: Medicines and Healthcare Products Regulatory Agency Portugal: INFARMED, National Authority of Medicines and Health Products, IP

Japan: Pharmaceuticals and Medical Devices Agency
Russia: Ministry of Health of the Russian Federation

Keywords provided by Ariad Pharmaceuticals:

Chronic Phase Chronic Myeloid Leukemia
CML
Leukemia
Leukemia, Myeloid
Leukemia, Myelogenous, Chronic, BCR-ABL Positive
Neoplasms by Histologic Type
Neoplasms
Myeloproliferative Disorders
Bone Marrow Diseases
Hematologic Diseases
CP-CML

Additional relevant MeSH terms:

Leukemia
Leukemia, Myeloid
Leukemia, Myelogenous, Chronic, BCR-ABL Positive
Leukemia, Myeloid, Chronic-Phase
Neoplasms by Histologic Type
Neoplasms
Myeloproliferative Disorders
Bone Marrow Diseases
Hematologic Diseases
Ponatinib
Antineoplastic Agents
Protein Kinase Inhibitors
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action

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