PONATINIB for Chronic Myeloid Leukemia (CML) Evaluation and Ph+ Acute Lymphoblastic Leukemia (ALL) (PACE)

This study is ongoing, but not recruiting participants.

First Received on September 20, 2010.  Last Updated on July 6, 2012  History of Changes

<table>
<thead>
<tr>
<th>Sponsor:</th>
<th>Ariad Pharmaceuticals</th>
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<tbody>
<tr>
<td>Information provided by (Responsible Party):</td>
<td>Ariad Pharmaceuticals (Ariad Pharmaceuticals)</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier:</td>
<td>NCT01207440</td>
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**Purpose**

The purpose of this study is to determine the efficacy of ponatinib in patients with chronic myeloid leukemia (CML) in chronic phase (CP), accelerated phase (AP) or blast phase (BP) or with Ph positive (Ph+) acute lymphoblastic leukemia (ALL) who either are resistant or intolerant to either dasatinib or nilotinib, or have the T315I mutation.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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<tbody>
<tr>
<td>Chronic Myeloid Leukemia (CML)</td>
<td>Drug: Ponatinib (AP24534)</td>
<td>Phase 2</td>
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<tr>
<td>Ph+ Acute Lymphoblastic Leukemia (ALL)</td>
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Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Pivotal Phase 2 Trial of Ponatinib (AP24534) in Patients With Refractory Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia

Resource links provided by NLM:
- MedlinePlus related topics: Acute Lymphocytic Leukemia, Chronic Lymphocytic Leukemia
- Chronic Myeloid Leukemia
- Leukemia
- U.S. FDA Resources

Further study details as provided by Ariad Pharmaceuticals:

Primary Outcome Measures:

- Major cytogenetic response (MCyR) CP patients, and Major Hematologic Response (MaHR) AP/BP and Ph+ ALL patients [Time Frame: up to 24 months after first dose]
  [Designated as safety issue: No]
  1. For CML patients in CP at study entry: major cytogenetic response (MCyR), defined as complete cytogenetic response (CCyR) or partial cytogenetic response (PcYR). CP patients in CCyR are not eligible for this study.
  2. For CML patients in AP at study entry: major hematologic response (MaHR), defined as complete hematologic response (CHR) or no evidence of leukemia (NEL). AP patients in MaHR are not eligible for this study.
  3. For CML patients in BP at study entry or Ph+ ALL patients: MaHR, consisting of CHR or NEL. BP and Ph+ ALL patients in MaHR are not
eligible for this study.

Secondary Outcome Measures:

- Clinical response, molecular response, clinical outcomes and safety [Time Frame: up to 24 months after first dose] [Designated as safety issue: No]
  1. For CML patients in CP:
     1. Hematologic responses: CHR;
     2. Cytogenetic responses: confirmed MCR; and
  2. For CML patients in AP or BP or Ph+ ALL patients:
     1. Cytogenetic responses: CCyR, PCyR, confirmed MCR; and
     2. Molecular responses: MMR.
  3. For all patients: time to response, duration of response, progression free survival, and overall survival.
  4. For all patients: safety and tolerability.

Estimated Enrollment: 440
Study Start Date: September 2010
Estimated Study Completion Date: October 2021
Estimated Primary Completion Date: October 2021 (Final data collection date for primary outcome measure)

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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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| Experimental: CML | Drug: Ponatinib (AP24534)  
                  | 45 mg tablet taken orally once daily  
                  | Other Name: AP24534                      |

Detailed Description:

The preliminary analysis of the phase 1 clinical trial revealed evidence of clinical antitumor activity in patients with resistance to approved second-generation tyrosine kinase inhibitors (TKI), dasatinib and nilotinib, including patients with the T315I mutation of BCR-ABL. This study, taken together with the strong preclinical data that characterize ponatinib, provides the rationale for moving to a pivotal phase 2 trial of this agent in a population of patients with chronic myeloid leukemia (CML) and Ph+ Acute Lymphoblastic Leukemia (ALL) who are resistant or intolerant to prior TKI therapy and in those patients with the T315I mutation.

Eligibility

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

Criteria

Inclusion Criteria:

- Previously treated with and developed resistance or intolerance to dasatinib or nilotinib, or developed the T315I mutation after any TKI therapy including imatinib
- ≥18 years old
- ECOG performance status ≤2
- Normal pancreatic function
- QTcF interval ≤450 ms for males and ≤470 ms for females
- Adequate renal and hepatic function
- Minimum life expectancy of ≥3 months
- Provide written informed consent
- Negative pregnancy test and agree to use effective form of contraception (if applicable)

Exclusion Criteria:

- Received prior tyrosine kinase inhibitor (TKI) treatment within 7 days prior to receiving the first dose of ponatinib
- Received other therapies as follows:
  1. For CML chronic phase (CP) and accelerated phase (AP) patients, received hydroxyurea
or anagrelide within 24 hours prior to receiving the first dose of ponatinib; interferon, cytarabine, or immunotherapy within 14 days prior to first dose of ponatinib; or any other cytotoxic chemotherapy, radiotherapy, or investigational therapy within 28 days prior to receiving the first dose of ponatinib.

2. For CML blast phase (BP) patients, received chemotherapy within 14 days prior to the first dose of ponatinib.

3. For Ph+ ALL patients, received corticosteroids within 24 hours before the first dose of ponatinib; or vincristine within 7 days prior to the first dose of ponatinib; or received other chemotherapy within 14 days prior to the first dose of ponatinib.

4. All patients are excluded if they have not recovered from adverse events except alopecia resulting from any prior treatments administered.

- Taking medications that are known to be associated with torsades de pointes
- Previously treated with ponatinib
- Underwent stem cell transplant <60 days prior to receiving first dose of ponatinib
- Evidence of on-going graft versus-host disease (GVHD), or GVHD requiring immunosuppressive therapy
- Require concurrent treatment with immunosuppressive agents
- Have active Central Nervous System (CNS) disease
- Have significant or active cardiovascular disease
- Have a significant bleeding disorder unrelated to CML or Ph+ALL
- Have a history of pancreatitis or alcohol abuse
- Have uncontrolled hypertriglyceridemia (triglycerides >450 mg/dL)
- Underwent major surgery within 14 days prior to first dose of ponatinib
- Have ongoing or active infection
- Have malabsorption syndrome or other gastrointestinal illness that could affect absorption of ponatinib
- Diagnosed with another primary malignancy in the past 3 years
- Pregnant or lactating
- Suffer from any other condition or illness that would compromise safety

**Contacts and Locations**

Please refer to this study by its ClinicalTrials.gov identifier: NCT01207440

Show 68 Study Locations

**Sponsors and Collaborators**

Ariad Pharmaceuticals

**More Information**

No publications provided

Responsible Party: Ariad Pharmaceuticals (Ariad Pharmaceuticals)

ClinicalTrials.gov Identifier: NCT01207440

Other Study ID Numbers: AP24534-10-201

Study First Received: September 20, 2010

Last Updated: July 6, 2012

Health Authority: United States: Food and Drug Administration

Keywords provided by Ariad Pharmaceuticals:

- CML
- ALL
- PH
- ponatinib
- PAGE
- Ph+ ALL

Additional relevant MeSH terms:

- Leukemia
- Leukemia, Lymphoid
- Precursor Cell Lymphoblastic Leukemia-Lymphoma
- Leukemia, Myeloid
- Leukemia, Myelogenous, Chronic, BCR-ABL
- Positive
- Neoplasms by Histologic Type
- Neoplasms
- Lymphoproliferative Disorders
- Lymphatic Diseases
- Immunoproliferative Disorders
- Immune System Diseases
- Myeloproliferative Disorders
- Bone Marrow Diseases
- Hematologic Diseases
