Trial record **1 of 1** for: CABL001A2301

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Study of Efficacy of CML-CP Patients Treated With ABL001 Versus Bosutinib, Previously Treated With 2 or More TKIs

This study is currently recruiting participants.

See Contacts and Locations

Verified November 2017 by Novartis (Novartis Pharmaceuticals)

Sponsor:
Novartis Pharmaceuticals

ClinicalTrials.gov Identifier:
NCT03106779

First Posted: April 10, 2017
Last Update Posted: November 10, 2017

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

Purpose

The purpose of this pivotal study is to compare the efficacy of ABL001 with that of bosutinib in the treatment of patients with CML-CP having previously been treated with a minimum of two prior ATP-binding site TKIs with BCR-ABL ratios ≥ 1% IS at screening.

Condition	Intervention	Phase
Chronic Myelogenous Leukemia	Drug: ABL001 Drug: Bosutinib	Phase 3

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Official Title: A Phase 3, Multi-center, Open-label, Randomized Study of Oral ABL001 Versus Bosutinib in Patients With Chronic Myelogenous Leukemia in Chronic Phase (CML-CP), Previously Treated With 2 or More Tyrosine Kinase Inhibitors

Resource links provided by NLM:

Genetics Home Reference related topics: chronic myeloid leukemia

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Bosutinib

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 Novartis (Novartis Pharmaceuticals):

Primary Outcome Measures:

- Major Molecular Response (MMR) rate [Time Frame: at 24 weeks]

  To compare the MMR rate of ABL001 versus bosutinib

Secondary Outcome Measures:

- Major Molecular Response (MMR) rate [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Complete Cytogenetic response rate [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib. Cytogenic response will include Complete, Partial, Major, Minor, Minimal and no response.

- Time to MMR [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Duration of MMR [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Time to CCyR [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Duration of CCyR [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Time to treatment failure [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Progression free survival [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Overall survival [Time Frame: 96 weeks after the last patient received the first study dose]

  To compare additional parameters of the efficacy of ABL001 versus bosutinib

- Trough plasma concentrations [Time Frame: 96 weeks after the last patient received the first study dose]

To characterize the PK of ABL001 in the CML-CP population

- PK parameter: Cmax, [Time Frame: 96 weeks after the last patient received the first study dose]

  To characterize the PK of ABL001 in the CML-CP population

- PK parameter: Tmax [Time Frame: 96 weeks after the last patient received the first study dose]

  To characterize the PK of ABL001 in the CML-CP population

- PK parameter: AUC0-12h [Time Frame: 96 weeks after the last patient received the first study dose]

  To characterize the PK of ABL001 in the CML-CP population

- PK parameter: CL/F [Time Frame: 96 weeks after the last patient received the first study dose]

  To characterize the PK of ABL001 in the CML-CP population

Estimated Enrollment:	222
Actual Study Start Date:	October 26, 2017
Estimated Study Completion Date:	March 22, 2024
Estimated Primary Completion Date:	March 22, 2024 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: ABL001 patients will be treated with ABL001	Drug: ABL001 40 mg tablets will be taken orally twice a day (BID) Other Name: asciminib
Active Comparator: Bosutinib patients will be treated with bosutinib	Drug: Bosutinib 500 mg tablets will be taken orally once daily (QD)

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:

Male or female patients with a diagnosis of CML-CP ≥ 18 years of age

Patients must meet all of the following laboratory values at the screening visit:

- < 15% blasts in peripheral blood and bone marrow
- < 30% blasts plus promyelocytes in peripheral blood and bone marrow
- < 20% basophils in the peripheral blood
- ≥ 50 x 109/L (≥ 50,000/mm3) platelets
- Transient prior therapy related thrombocytopenia (< 50,000/mm3 for ≤ 30 days prior to screening) is acceptable
- No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly

BCR-ABL ratio ≥ 1% IS according to central laboratory at the screening examination

Prior treatment with a minimum of 2 prior ATP-binding site TKIs (i.e. imatinib, nilotinib, dasatinib, radotinib or ponatinib)

Failure or intolerance to the last previous TKI therapy at the time of screening (adapted from the 2013 ELN Guidelines Bacarrani 2013)

- Failure is defined for CML-CP patients (CP at the time of initiation of last therapy) as follows. Patients must meet at least 1 of the following criteria.
- Three months after the initiation of therapy: No CHR or > 95% Ph+ metaphases
- Six months after the initiation of therapy: BCR-ABL ratio > 10% IS and/or > 65% Ph+ metaphases
- Twelve months after initiation of therapy: BCR-ABL ratio > 10% IS and/or > 35% Ph+ metaphases

- At any time after the initiation of therapy, loss of CHR, CCyR or PCyR
- At any time after the initiation of therapy, the development of new BCR-ABL mutations
- At any time after the initiation of therapy, confirmed loss of MMR in 2 consecutive tests, of which one must have a BCR-ABL ratio ≥ 1% IS
- At any time after the initiation of therapy, new clonal chromosome abnormalities in Ph+ cells: CCA/Ph+
- Intolerance is defined as:
- Non-hematologic intolerance: Patients with grade 3 or 4 toxicity while on therapy, or with persistent grade 2 toxicity, unresponsive to optimal management, including dose adjustments (unless dose reduction is not considered in the best interest of the patient if response is already suboptimal)
- Hematologic intolerance: Patients with grade 3 or 4 toxicity (absolute neutrophil count [ANC] or platelets) while on therapy that is recurrent after dose reduction to the lowest doses recommended by manufacturer

Exclusion Criteria:

Known presence of the T315I or V299L mutation at any time prior to study entry Known second chronic phase of CML after previous progression to AP/BC Previous treatment with a hematopoietic stem-cell transplantation Patient planning to undergo allogeneic hematopoietic stem cell transplantation

Cardiac or cardiac repolarization abnormality, including any of the following:

- History within 6 months prior to starting study treatment of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG)
- Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third degree AV block)
- QTcF at screening ≥450 ms (male patients), ≥460 ms (female patients)
- Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following:
- Risk factors for Torsades de Pointes (TdP) including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia
- Concomitant medication(s) with a known risk to prolong the QT interval and/or known to cause Torsades de Pointes that cannot be discontinued or replaced 7 days prior to starting study drug by safe alternative medication.
- Inability to determine the QTcF interval

- Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol (e.g. uncontrolled diabetes, active or uncontrolled infection, pulmonary hypertension)
- History of acute pancreatitis within 1 year of study entry or past medical history of chronic pancreatitis
- History of acute or chronic liver disease
- Treatment with medications that meet one of the following criteria and that cannot be discontinued at least one week prior to the start of treatment with study treatment
- Moderate or strong inducers of CYP3A
- Moderate or strong inhibitors of CYP3A and/or P-gp
- Substrates of CYP3A4/5, CYP2C8, or CYP2C9 with narrow therapeutic index
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 3 days after last dose of ABL001. Highly effective contraception methods include:
- Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception
- Female sterilization (have had surgical bilateral oophorectomy (with or without hysterectomy) total hysterectomy or tubal ligation at least six weeks before taking study treatment). In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment
- Male sterilization (at least 6 months prior to screening). The vasectomized male partner should be the sole partner for that subject.
- Use of oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception.
- In case of use of oral contraception women should have been stable on the same pill for a minimum of 3 months before taking study treatment.
- Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.

- Sexually active males unless they use a condom during intercourse while taking the drug during treatment and for 3 days after stopping treatment and should not father a child in this period. A condom is required to be used also by vasectomized men as well as during intercourse with a male partner in order to prevent delivery of the drug via semen.

Contacts and Locations

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): ***NCT03106779***

Contacts

Contact: Novartis Pharmaceuticals 1-888-669-6682 novartis.email@novartis.com

Contact: Novartis Pharmaceuticals +41613241111 novartis.email@novartis.com

Locations

United States, California

City of Hope **Recruiting**
Duarte, California, United States, 91010
Contact: Annette Brown 626-930-5452 abrown@coh.org
Principal Investigator: David S Snyder

United States, Missouri

Washington U School of Medicine, Center for Clinical Studies Main Site **Recruiting**
Saint Louis, Missouri, United States, 63110
Contact: Melissa Haley haleym@wustl.edu
Principal Investigator: Camille N. Abboud

Australia, Victoria

Novartis Investigative Site **Recruiting**
Melbourne, Victoria, Australia, 3000

Australia, Western Australia

Recruiting

Novartis Investigative Site
Murdoch, Western Australia, Australia, 6150

Canada, Quebec

Novartis Investigative Site **Recruiting**
Montreal, Quebec, Canada, H3T 1E2

Germany

Novartis Investigative Site **Recruiting**
Mannheim, Baden-Württemberg, Germany, 68305

Israel

Novartis Investigative Site **Recruiting**
Haifa, Israel, 3525408

Novartis Investigative Site **Recruiting**
Zrifin, Israel, 70300

Spain

Novartis Investigative Site **Recruiting**
Madrid, Spain, 28034

Sponsors and Collaborators

Novartis Pharmaceuticals

Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

More Information

Responsible Party:	Novartis Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT03106779 History of Changes
Other Study ID Numbers:	**CABL001A2301**
First Submitted:	March 9, 2017
First Posted:	April 10, 2017
Last Update Posted:	November 10, 2017
Last Verified:	November 2017

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:	Undecided
Plan Description:	Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from

eligible studies. These requests are reviewed and approved by an independent expert panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data is currently available according to the process described on www.clinicalstudydatarequest.com

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

Keywords provided by Novartis (Novartis Pharmaceuticals):

Phase 3
Chronic Myelogenous Leukemia
CML
bosutinib
ABL001
tyrosine kinase inhibitor
Chronic myelogenous leukemia (CML)
chronic myeloid leukemia (CML)
chronic myelocytic leukemia (CML)
chronic granulocytic leukemia (CGL)
cancer of the white blood cells
clonal bone marrow stem cell disorder
proliferation of mature granulocytes

Additional relevant MeSH terms:

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