Open-Label Study Evaluating Dasatinib Therapy Discontinuation in Patients With Chronic Phase Chronic Myeloid Leukemia With Stable Complete Molecular Response (DASFREE)

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

Verified July 2015 by Bristol-Myers Squibb

Sponsor:
Bristol-Myers Squibb

Collaborators:
ICON plc
PPD
Molecular MD
European Organisation for Research and Treatment of Cancer - EORTC
MultiPharma
Steering Committee

Information provided by (Responsible Party):
Bristol-Myers Squibb

ClinicalTrials.gov Identifier:
NCT01850004

First received: May 8, 2013
Last updated: September 3, 2015
Last verified: July 2015
History of Changes

Purpose

The study purpose is to test the hypothesis that Chronic Phase Chronic Myeloid Leukemia (CP-CML) patients with stable Complete Molecular Response (CMR)who discontinue Dasatinib treatment are able to maintain a sustained remission in the long-term, with undetectable or minimally detectable BCR-ABL residual disease.

Condition	Intervention	Phase
Chronic Phase Chronic Myeloid Leukemia	Drug: Dasatinib	Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label

Official Title: Open-Label Single Arm Phase 2 Study Evaluating Dasatinib Therapy Discontinuation In Patients With Chronic Phase Chronic Myeloid Leukemia (CP-CML) With Stable Complete Molecular Response (CMR) DASFREE

Resource links provided by NLM:

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Dasatinib

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

U.S. FDA Resources

Further study details as provided by Bristol-Myers Squibb:

Primary Outcome Measures:

- MMR rate at 12 months [Time Frame: At 12 months after Dasatinib discontinuation] [Designated as safety issue: No]

  Major Molecular Response (MMR) rate at 12 months is the proportion of subjects who maintain MMR (BCR-ABL transcripts < 0.1% on International Scale (IS)) at 12 months after Dasatinib discontinuation without re-starting Dasatinib treatment in the enrolled subjects in the study

Secondary Outcome Measures:

- Event-free survival (EFS) after Dasatinib discontinuation [Time Frame: At 12 months after Dasatinib discontinuation] [Designated as safety issue: Yes]

  EFS is defined as survival w ith no molecular relapse, including no loss of MMR

- Relapse-free survival (RFS) after Dasatinib discontinuation [Time Frame: At 6,12,18, 24 months and every 6 months thereafter up to 5 years] [Designated as safety issue: Yes]

  Relapse is defined as any of the follow ing events w hile a subject is on study: the loss of MMR, Complete Cytogenetic Response (CCyR), Complete Hematologic Response (CHR) or progression to advanced/blastic phase. RFS is defined as the time from Dasatinib treatment discontinuation to the date of relapse

- Assessment of BCR-ABL kinetics for subjects w ho experience loss of Complete Molecular Response (CMR) but not MMR [Time Frame: Monthly in the first year and every 3 months thereafter up to 5 years] [Designated as safety issue: No]
- Assessment of BCR-ABL kinetics in subjects in CMR or less w ith measurable levels [Time Frame: Monthly in the first year and every 3 months thereafter up to 5 years] [Designated as safety issue: No]
- Rate of transformation to AP/BC [Time Frame: Up to 5 years or death date] [Designated as safety issue: Yes]

  Accelerated Phase (AP) is defined as Blasts in Peripheral Blood (PB) or Bone Marrow (BM) 15-29%; Blast+promyelocytes ≥30% w ith blasts < 30% or Additional Chromosomal Abnormalities (ACA) in Ph+ cells (clonal progression), or basophils in blood ≥ 20% or platelets <100 x 10(9)/L unrelated to therapy Blastic Phase or Crisis (BP/BC) is defined as Blasts in PB or BM ≥30%, or extramedullary blast cell involvement (w ith the exception of spleen and liver)

- Progression Free Survival (PFS) [Time Frame: Up to 5 years or death date] [Designated as safety issue: Yes]

  Progression-free survival (PFS) is defined as overall survival plus the additional events progression to accelerated phase or blast crisis

- Rate of transformation to OS [Time Frame: Up to 5 years or death date] [Designated as safety issue: Yes]

  Overall survival (OS) is defined as the time betw een first dose date and death date

Estimated Enrollment:	79
Study Start Date:	October 2013
Estimated Study Completion Date:	July 2021
Estimated Primary Completion Date:	July 2021 (Final data collection date for primary outcome measure)

Arms	Assigned Interv entions
Experimental: Dasatinib Dasatinib 20, 50, 80, 100 and 140 mg tablets by mouth, once daily, up to 60 months	Drug: Dasatinib Other Name: Sprycel

Detailed Description:

Primary Purpose: Protocol designed to evaluate remission of disease after treatment discontinuation. Treatment re-started if relapse occurs

Eligibility

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

Criteria

For more information regarding BMS clinical trial participation, please visit w w w.BMSStudyConnect.com

Inclusion Criteria:

- Signed Written Informed Consent a. Patients must be informed of the investigational nature of this study and of alternative standard therapeutic options and must provide w ritten informed consent
- Target Population
  a. Men and w omen diagnosed w ith CP-CML, on treatment w ith dasatinib for a minimum of 2 years at the time of enrollment and in dasatinib -induced complete molecular remission (defined as ≤ 0.0032% or ≥ 4.5 log reduction of BCR-ABL transcript as determined by local standards) ongoing for at least 1 year prior to study entry 1. Patients are eligible for the screening assessment from the central lab if they have been in stable dasatinib induced CMR for a minimum of nine months, documented by at least three assessments, conducted 2 - 6.5 months apart, at a local lab. The first screening assessment conducted at the central lab w ill be repeated after three months, if the first assessment confirms CMR (MR 4.5). Patients are eligible for enrollment if both assessments from the central lab confirm MR4.5. For any patient not eligible for enrollment on the basis of a central laboratory test that does not confirm CMR, rescreening is allow ed 9 months after (or longer) from the last central lab screening failure. These patients must have documented stable CMR at the local lab, and must meet all other criteria, before rescreening.
  b. Subjects w ho have received dasatinib beyond first or second line treatment and meet other enrollment criteria are eligible for the study provided prior Tyrosine-kinase inhibitors (TKI) w ere discontinued due to intolerance or lack efficacy, although only one instance of lack

of efficacy to TKI is allowed.

c. Eastern Co-Operative Group (ECOG) Performance Status (PS) of 0-1

d. Life expectancy of > 1 year

e. Adequate renal function defined as serum creatinine ≤ 3.0 times the institutional ULN

f. Adequate hepatic function defined as: total bilirubin ≤ 3.0 times the institutional ULN; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 5 times the institutional upper limit of normal (ULN). In cases where the patient needs to restart dasatinib therapy, caution will be used in case of hepatic impairment.

g. Serum Na, K, Mg, and total serum Ca or ionized Ca levels must be greater than or equal to the institutional lower limit of normal. Patients with low K, Mg levels, total serum Ca and/or ionized Ca may be repleted to allow for protocol entry. Rescreening is permitted in the event of temporary biochemical abnormalities.

- Age and Reproductive Status

a. Men and women, ages ≥18

b. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test [minimum sensitivity 25 IU/L or equivalent units of Human Chorionic Gonadotropin (HCG)] within 24 hours prior to the restart of study drug

c. Women must not be breastfeeding

d. WOCBP must agree to follow instructions for method(s) of contraception at the restart of treatment with study drug (dasatinib) and for the duration treatment plus 30 days (duration of ovulatory cycle) for a total of 30 days post-treatment completion

e. Men who are sexually active with WOCBP must agree to follow instructions for method(s) of contraception for 90 days after study entry (withdrawal of dasatinib), at restart of study drug (dasatinib) and for the duration of treatment with study drug (dasatinib) plus 90 days (duration of sperm turnover) for a total of 90 days post-treatment completion Investigators shall counsel WOCBP and male subjects who are sexually active with WOCBP on the importance of pregnancy prevention and the implications of an unexpected pregnancy. Investigators shall advise WOCBP and male subjects who are sexually active with WOCBP on the use of highly effective methods of contraception. Highly effective methods of contraception have a failure rate of < 1% per year when used consistently and correctly At a minimum, subjects must agree to the use of two methods of contraception, with one method being highly effective and the other method being either highly effective or less effective

f. Azoospermic males and WOCBP who are continuously not heterosexually active are exempt from contraceptive requirements. However WOCBP must still undergo pregnancy testing as described in these sections

Exclusion Criteria:

- Target Disease Exceptions

a. Patients who have not achieved a 1-log reduction in BCR-ABL transcript levels compared with baseline as determined by local standards or > 10% IS [International Standard]) documented at 3.0-6.5 months since the initial start of dasatinib therapy.

b. Patients who have previously undergone hematopoietic stem cell transplantation (SCT) or who are scheduled for SCT

c. Previous diagnosis of CML accelerated phase or blast crisis

- Medical History and Concurrent Diseases

a. Prior or concurrent malignancy, except the following:

- Curatively treated basal cell or squamous cell skin cancer
- Cervical carcinoma in situ
- Adequately treated Stage I or II cancer from which the subject is currently in complete remission
- Any other cancer from which the subject has been disease free for 3 years

b. A serious uncontrolled medical disorder or active infection that would impair the ability of the subject to receive protocol therapy in case re-initiation of dasatinib is needed.

c. Uncontrolled or significant cardiovascular disease, including any of the following:

- Diagnosed or suspected congenital long QT syndrome
- Any history of significant ventricular arrhythmias for example ventricular tachycardia (BT), ventricular fibrillation (VF), and Torsade de Points (TdP)
- Prolonged QT Interval Corrected (QTc) interval on pre-entry electrocardiogram that is considered clinically significant according to investigator's criteria
- Any history of second- or third-degree heart block (may be eligible if the subject currently has a pacemaker)

d. Subjects with prior history of pericardial effusion or pleural effusion that required thoracentesis are excluded. Subjects with prior history of pericardial or pleural effusion that was clinically manageable and a maintained CMR for ≥ 1 year on a stable dose of dasatinib are allowed.

e. History of significant bleeding disorder unrelated to CML, including

- Diagnosed congenital bleeding disorders (e.g., von Willebrand's disease)
- Diagnosed acquired bleeding disorder within one year (e.g., acquired anti-factor VIII antibodies)

- Physical and Laboratory Test Findings
- Allergies and Adverse Drug Reaction a. Subjects with known hypersensitivity to excipients of Dasatinib tablets (Tablet core:lactose monohydrate, microcrystalline cellulose, croscarmellose sodium; hydroxypropyl cellulose, magnesium stearate; Film-coating: hypromellose titanium dioxide macrogol 400)
- Sex and Reproductive Status

a. Patients who are pregnant or breastfeeding or likely to become pregnant

b. Men w hose partner is unw illing or unable to avoid pregnancy

- Other Exclusion Criteria
  a. Patients w ith a history of non-compliance to CML treatment and monitoring requirements
  b. Prisoners or subjects w ho are involuntarily incarcerated
  c. Subjects w ho are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith 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: NCT01850004

Contacts

Contact: Recruiting sites have contact information. Please contact the sites directly. If there is no contact information, please email: Clinical.Trials@bms.co

Contact: First line of the email MUST contain NCT# and Site #.

Locations

United States, California

City Of Hope Medical Center — **Recruiting**
Duarte, California, United States, 91010
Contact: Claudia Aceves, Site 0006 503-413-1600

David Geffen School Of Medicine At Ucla — **Recruiting**
Los Angeles, California, United States, 90095
Contact: Ronald Paquette, Site 0029

Ucsf Division Of Hematology And Oncology — **Recruiting**
San Francisco, California, United States, 94143
Contact: Neil P. Shah, Site 0001 415-476-3303

United States, New Jersey

John Theurer Cancer Center At Hackensack University Medical Center — **Recruiting**
Hackensack, New Jersey, United States, 07601
Contact: Stefan Faderl, Site 0024 551-996-5900

United States, New York

Columbia University Medical Center (Cumc) — **Recruiting**
New York, New York, United States, 10032
Contact: Mark Heaney, Site 0028 646-317-5199

United States, Texas

Baylor Charles A. Sammons Cancer Center — **Recruiting**
Dallas, Texas, United States, 75246
Contact: Moshe Levy, Site 0011 214-370-1065

The University Of Texas Md Anderson Cancer Center — **Recruiting**
Houston, Texas, United States, 77030
Contact: Jorge E Cortes, Site 0023 713-563-2634

Canada, Ontario

Local Institution — **Recruiting**
Toronto, Ontario, Canada, M5G 2M9
Contact: Site 0005

France

Local Institution — **Recruiting**
Paris Cedex 10, France, 75475
Contact: Site 0012

Local Institution — **Recruiting**
Pessac, France, 33604
Contact: Site 0003

Local Institution — **Active, not recruiting**
Pierre Benite, France, 69310

Local Institution — **Recruiting**
Vandoeuvre-les-Nancy CEDEX, France, 54511

Contact: Site 0002

Germany

Local Institution — **Recruiting**
Aachen, Germany, 52074
Contact: Site 0026

Local Institution — **Recruiting**
Berlin, Germany, 13353
Contact: Site 0020

Local Institution — **Recruiting**
Mannheim, Germany, 68169
Contact: Site 0021

Local Institution — **Recruiting**
Rostock, Germany, 18055
Contact: Site 0019

Local Institution — **Not yet recruiting**
Ulm, Germany, 89081
Contact: Site 0022

Italy

Local Institution — **Recruiting**
Catania, Italy, 95124
Contact: Site 0025

Local Institution — **Recruiting**
Firenze, Italy, 50134
Contact: Site 0017

Local Institution — **Recruiting**
Napoli, Italy, 80131
Contact: Site 0027

Local Institution — **Recruiting**
Orbassano, Italy, 10043
Contact: Site 0015

Local Institution — **Recruiting**
Roma, Italy, 00144
Contact: Site 0018

Local Institution — **Recruiting**
Roma, Italy, 00161
Contact: Site 0016

Spain

Local Institution — **Recruiting**
Las Palmas de Gran Canaria, Spain, 35010
Contact: Site 0009

Local Institution — **Recruiting**
Madrid, Spain, 28034
Contact: Site 0010

Local Institution — **Recruiting**
Malaga, Spain, 29010
Contact: Site 0008

Local Institution — **Recruiting**
Oviedo, Spain, 33011
Contact: Site 0014

Sponsors and Collaborators

Bristol-Myers Squibb

ICON plc

PPD

Molecular MD

European Organisation for Research and Treatment of Cancer - EORTC

MultiPharma

Steering Committee

Investigators

Study Director: Bristol-Myers Squibb Bristol-Myers Squibb

More Information

Additional Information:

BMS Clinical Trial Information

BMS clinical trial educational resource

Investigator Inquiry form

FDA Safety Alerts and Recalls

No publications provided

Responsible Party:	Bristol-Myers Squibb
ClinicalTrials.gov Identifier:	NCT01850004 History of Changes
Other Study ID Numbers:	**CA180-406**, 2012-001421-27
Study First Received:	May 8, 2013
Last Updated:	September 3, 2015
Health Authority:	United States: Institutional Review Board United States: Food and Drug Administration Canada: Institutional Review Board Canada: Health Canada France: Committee for the Protection of Personnes France: Agence Nationale de Sécurité du Médicament et des produits de santé Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices Italy: Ethics Committee Italy: The Italian Medicines Agency Spain: Spanish Agency of Medicines Spain: Ethics Committee

Additional relevant MeSH terms:

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

ClinicalTrials.gov processed this record on September 03, 2015