This study is ongoing, but not recruiting participants.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT01698905

First received: October 1, 2012
Last updated: May 28, 2015
Last verified: May 2015

Purpose

A clinical research study to find out if it is safe to stop the drug nilotinib (Tasigna) in chronic myeloid leukemia (CML) patients. Patients who started treatment with imatinib (Gleevec) when they were first diagnosed with CML, then switched to nilotinib (Tasigna) for at least 2 years with the combined time on imatinib (Gleevec) and nilotinib (Tasigna) for at least 3 years and have very small amount of leukemia cells remaining after the nilotinib (Tasigna) treatment will qualify for the study.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>Drug: nilotinib</td>
<td>Phase 2</td>
</tr>
</tbody>
</table>

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

Official Title: A Phase II, Single Arm, Open Label Study of Treatment-free Remission in Chronic Myeloid Leukemia (CML) Chronic Phase (CP) Patients After Achieving Sustained MR4.5 on Nilotinib

Resource links provided by NLM:

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Nilotinib

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 Novartis:

Primary Outcome Measures:

- No documented confirmed loss of MR4, no documented loss of MMR and no re-starting of nilotinib therapy [Time Frame: First 12 months following nilotinib cessation.][Designated as safety issue: No]

Proportion of patients without confirmed loss of MR4 or loss of MMR within 12 months following nilotinib TFR is calculated by dividing the number of patients without documented confirmed loss of MR4, no documented loss of MMR and no re-starting of nilotinib therapy in the first 12 months after starting nilotinib TFR phase by the number of patients who entered nilotinib TFR phase.
Secondary Outcome Measures:

- No documented confirmed loss of MR4, no documented loss of MMR and no re-starting of nilotinib therapy in the first 24, 36, and 48 months following nilotinib cessation. [Time Frame: 24, 36 and 48 months following nilotinib cessation] [Designated as safety issue: No]

  The proportion of patients without confirmed loss of MR4 or loss of MMR within 24, 36, and 48 months following nilotinib cessation is calculated by dividing the number of patients with no documented confirmed loss of MR4, no documented loss of MMR and no re-starting of nilotinib therapy in the first 24, 36, and 48 months after starting nilotinib TFR phase by the number of patients who entered the nilotinib TFR phase.

- Progression to AP/BC or death where the "failure" event is the earliest occurrence of the following event: progression to AP/BC or death from any cause. [Time Frame: study duration] [Designated as safety issue: Yes]

  Kaplan-Meier (KM) estimation of PFS. PFS is measured from the date of start of nilotinib TFR phase to the date of the earliest of the event: progression to AP/BC, or death from any cause. Patients not known to have recurred or died on or before the cut-off date for the KM analysis will have their PFS interval right-censored at the earlier of the date of their last assessment (cytogenetic, hematologic or extramedullary) for patients who are still on study and at the date of last contact for patients who are in follow-up.

- Treatment free survival (TFS) defined as lack of any of the following events: loss of MMR, confirmed loss of MR4, re-start of Nilotinib treatment, progression to AP/BC or death from any cause. [Time Frame: study duration] [Designated as safety issue: Yes]

  TFS is measured from the date of the start of the nilotinib TFR phase to the date of the earliest of the following events: loss of MMR, confirmed loss of MR4, re-start of nilotinib treatment, progression to AP/BC or death from any cause. Patients not known to have had any of the events or died on or before the cut-off date for the KM analysis will have their TFS interval right-censored at the earlier of the date of their last assessment (PCR, cytogenetic, hematologic or extramedullary) for patients who are still on study and at the date of last contact for patients who are in follow-up.

- Overall survival (OS) defined as the time from the date of cessation of nilotinib therapy to the date of death from any cause. [Time Frame: study duration] [Designated as safety issue: Yes]

  Kaplan-Meier (KM) estimation of OS. OS is measured from the date of start of nilotinib TFR phase to the date of death from any cause. If a patient is not known to have died, survival will be censored at the date of last contact.

- BCR-ABL transcript changes within 12 months after re-start of nilotinib therapy [Time Frame: within 12 months after re-start of nilotinib therapy] [Designated as safety issue: No]

  Descriptive statistics of BCR-ABL over time after re-start of nilotinib therapy.

Enrollment:

- 163

Study Start Date:

- December 2012

Estimated Study Completion Date:

- January 2019

Estimated Primary Completion Date:

- January 2019 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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<tbody>
<tr>
<td>Experimental:</td>
<td>Drug: nilotinib</td>
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<tr>
<td>nilotinib</td>
<td>Nilotinib will be labeled as AMN107 and supplied as 150 mg and/or 200 mg hard gelatin capsule. Nilotinib will not be dosed by body weight or body surface area. Nilotinib will be administered orally at 300 mg twice daily (BID) or 400 mg BID, at approximately 12 hour intervals, and must not be taken with food. The capsules should be swallowed whole with water. No food should be consumed for at least 2 hours before the dose is taken and no additional food should be consumed for at least one hour after the dose is taken. Patients who were previously treated with 400 mg BID, and required subsequent permanent dose reduction to 400 mg QD will be allowed to enter this study on the same dose, 400 mg once daily.</td>
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<tr>
<td>70 patients who maintain MR4.5 during the one year nilotinib consolidation phase will stop treatment when they enter the treatment-free remission (TFR) phase</td>
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</table>

Eligibility:

- Genders Eligible for Study: Both
- Accepts Healthy Volunteers: No

Criteria:

1. Male or female patients >= 18 years of age
2. ECOG Performance Status of 0, 1, or 2
3. Patient with diagnosis of BCR-ABL positive CML CP
4. Patient has received a minimum of 3 years of tyrosine kinase inhibitor treatment (first with imatinib (> 4 weeks) and then switched to nilotinib) since initial diagnosis
5. Patient has at least 2 years of nilotinib treatment prior to study entry.
6. Patient has achieved MR4.5 (local laboratory assessment) during nilotinib treatment, and determined by a Novartis designated central PCR lab assessment at screening
7. Adequate end organ function as defined by:
   - Direct bilirubin ≤ 1.5 x ULN except for i) patient with documented Gilbert's syndrome for whom any bilirubin value is allowed and ii) for patients with asymptomatic hyperbilirubinemia (liver transaminases and alkaline phosphatase within normal range)
   - SGOT (AST) and SGPT (ALT) < 3 x ULN (upper limit of normal)
   - Serum lipase ≤ 2 x ULN
   - Alkaline phosphatase ≤ 2.5 x ULN
   - Serum creatinine < 1.5 x ULN
8. Patients must have the following electrolyte values ≥ LLN (lower limit of normal) limits or corrected to within normal limits with supplements prior to the first dose of study medication:
   - Potassium
   - Magnesium
   - Total calcium (corrected for serum albumin)
9. Patients must have normal marrow function as defined below:
   - Absolute Neutrophil Count (ANC) ≥ 1.5 x 10⁹/L
   - Platelets ≥ 100 x 10⁹/L
   - Hemoglobin ≥ 9.0 g/dL
10. Written informed consent obtained prior to any screening procedures

Exclusion Criteria:
1. Prior AP, BC or allo-transplant
2. Patient has documented MR4.5 at the time when switched from imatinib to nilotinib
3. Patients with known atypical transcript
4. CML treatment resistant mutation(s) (T315I, E255K/V, Y253H, F359C/V) detected if a testing was done in the past (there is no requirement to perform mutation testing at study entry if it was not done in the past)
5. Dose reductions due to neutropenia or thrombocytopenia in the past 6 months
6. Patient ever attempted to permanently discontinue imatinib or nilotinib treatment
7. Known impaired cardiac function including any one of the following:
   - Inability to determine the QT interval on ECG
   - Complete left bundle branch block
   - Long QT syndrome or a known family history of long QT syndrome
   - History of or presence of clinically significant ventricular or atrial tachyarrhythmias
   - Clinically significant resting bradycardia
   - QTcF > 480 msec
   - History or clinical signs of myocardial infarction within 1 year prior to study entry
   - History of unstable angina within 1 year prior to study entry
   - Other clinically significant heart disease (e.g. uncontrolled congestive heart failure or uncontrolled hypertension)
8. 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 (defined as HbA1c > 9%), uncontrolled infection)
9. History of acute pancreatitis within 1 year prior to study entry or past medical history of chronic pancreatitis
10. Known presence of a significant congenital or acquired bleeding disorder unrelated to cancer
11. History of other active malignancy within 5 years prior to study entry with the exception of previous or concomitant basal cell skin cancer, previous cervical carcinoma in situ treated curatively
12. Patients who have not recovered from prior surgery
13. Treatment with other investigational agents (defined as not used in accordance with the approved indication) within 4 weeks of Day 1
14. Patients actively receiving therapy with strong CYP3A4 inhibitors and/or inducers, and the treatment cannot be either discontinued or switched to a different medication prior to study entry. See Appendix 14.1 for a list of these medications. This list may not be comprehensive.
15. Patients actively receiving therapy with herbal medicines that are strong CYP3A4 inhibitors and/or inducers, and the treatment cannot
be either discontinued or switched to a different medication prior to study entry. These herbal medicines may include Echinacea, (including E. purpurea, E. angustifolia and E. pallida), Piperine, Artemisinin, St. John's Wort, and Ginkgo.

16. Patients who are currently receiving treatment with any medications that have the potential to prolong the QT interval and the treatment cannot be either safely discontinued or switched to a different medication prior to study entry. (Please see www.azcert.org/medical-pros/drug-lists/printable-drug-list.cfm for a list of agents that prolong the QT interval.)

17. Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug (e.g., ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection, or gastric bypass surgery)

18. Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.

19. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, must have a negative serum pregnancy test before initiation of study treatment and must also use highly effective methods of contraception while enrolled in the study. The use of highly effective contraception should continue for at least 14 days after the last dose of study treatment or until the last day of TFR/TFR-2, or for the duration of a monthly cycle of oral contraception, whichever is longer. Acceptable forms of highly effective contraception methods include: a. Total abstinence (when this is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception and male/female sterilization defined as:
   ◦ Female sterilization (have had surgical bilateral oophorectomy with or without 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 and documented by follow-up hormone level assessment
   ◦ Male sterilization (at least 6 months prior to screening). For female patients on the study, study participation assumes the vasectomized male partner is the sole partner for that patient or b. A combination of any two of the following (i+ii or i+iii or ii+iii): i) Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository ii) Use of oral, injected or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception iii) Placement of an intrauterine device (IUD) or intrauterine system (IUS)

Contact 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: NCT01698905

Show 68 Study Locations

Sponsors and Collaborators

Novartis Pharmaceuticals

Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

More Information

No publications provided

Responsible Party: Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier: NCT01698905 History of Changes

Other Study ID Numbers: CAMN107A2408

Study First Received: October 1, 2012

Last Updated: May 28, 2015

Health Authority: United States: Food and Drug Administration

Key words provided by Novartis:
Phase II, single arm, open label, nilotinib, treatment-free remission, MR4.5, confirmed loss of MR4, loss of MMR, Ph+ CML-CP

Additional relevant MeSH terms:
Leukemia, Myelogenous, Chronic, BCR-ABL Positive
Leukemia, Myeloid
Bone Marrow Diseases
Hematologic Diseases

Leukemia
Myeloproliferative Disorders
Neoplasms
Neoplasms by Histologic Type