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Trial record **1 of 1** for: 2010-024262-22

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Tasigna and Interferon Alpha Evaluation Initiated by the German Chronic Myeloid Leukemia Study Group - the TIGER Study

This study is currently recruiting participants.

Verified August 2013 *by University of Jena*

Sponsor:
University of Jena

Information provided by (Responsible Party):
Prof. Dr. med. Andreas Hochhaus, University of Jena

ClinicalTrials.gov Identifier:
NCT01657604

First received: July 9, 2012
Last updated: August 12, 2013
Last verified: August 2013
History of Changes

Full Text View | **Tabular View** | **No Study Results Posted** | Disclaimer | How to Read a Study Record

Purpose

Advances in Chronic Myeloid Leukemia (CML) therapy led to an expected survival prolongation of > 20 years after diagnosis. So far, discontinuation of tyrosine kinase inhibitors led to recurrence of disease in the majority of patients. The trial aims to improve treatment strategies in CML by improving induction therapy and deescalating maintenance therapy using low dose IFN as inducer of immunosurveillance. The trial will provide important data on the duration of active therapy in CML patients. Considering the rapidly increasing prevalence of CML this is of individual but also socioeconomic importance.

Condition	Intervention	Phase

	Chronic Myeloid Leukemia	Drug: Peginterferon α2b Drug: Nilotinib	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Diagnostic

Official Title: Treatment Optimization of Newly Diagnosed Ph/BCR-ABL Positive Patients With Chronic Myeloid Leukemia (CML) in Chronic Phase With Nilotinib vs. Nilotinib Plus Interferon Alpha Induction and Nilotinib or Interferon Alpha Maintenance Therapy

Resource links provided by NLM:

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Interferon Interferon Alfa-2a Nilotinib

U.S. FDA Resources

Further study details as provided by University of Jena:

Primary Outcome Measures:

- MMR rate at 18 months of nilotinib monotherapy versus nilotinib+pegylated interferon alpha [Time Frame: at least 18 months after start of study treatment] [Designated as safety issue: No]

  rate of MMR 18 months after randomization for each study treatment

- rate of continuous MMR after discontinuation of nilotinib versus pegylated interferon alpha [Time Frame: at least 12 months after stopping all therapy] [Designated as safety issue: No]

  rate of patients with molecular relapse (loss of MMR) 12 months after discontinuation of any treatment for CML

Secondary Outcome Measures:

- rate of CCyR and MMR [Time Frame: at 12, 18 and 24 months after start of treatment] [Designated as safety issue: No]
- Time to CCyR, MMR, MR4 and MR4.5 [Time Frame: date of randomization until time to endpoints or end of study duration (at least 36 months)] [Designated as safety issue: No]

  this time to-event endpoints give an impression of the velocity of drug response and of the time until a certain remission should be waited for

- rate of MR4 and MR4.5 during maintenance therapy and after discontinuation [Time Frame: start of maintenance therapy (after at least 24 months of treatment) until end of study duration (at least 36 months)] [Designated as safety issue: No]
- Progression-Free Survival (PFS) [Time Frame: at 12, 24 and 60 months after start of treatment] [Designated as safety issue: No]
- Rate of patients off treatment for at least 6 months [Time Frame: at 60 months after start of treatment] [Designated as safety issue: No]

  all patients and comparison of treatment arms

- safety and tolerability profile of nilotinib in comparison with nilotinib+pegylated interferon alpha and pegylated interferon alpha [Time Frame: time of first study treatment until 28 days after stop of study treatment (expected 36 months)] [Designated as safety issue: No]

  the time of risk is the time while receiving the therapy plus 28 days thereafter

- patients compliance to nilotinib based therapies [Time Frame: until stop of study treatment (at least 36 months)] [Designated as safety issue: No]
- quality of life during induction therapy with ilotinib versus nilotinib+pegylated interferon alpha and during maintenance therapy with nilotinib versus pegylated interferon alpha [Time Frame: during induction therapy (until at least 24 months), during maintenance therapy (until at least 36 months)] [Designated as safety issue: No]
- pharmacoeconomics of the treatment strategies [Time Frame: after end of study (expected in December 2020) (up to 8 years)] [Designated as safety issue: No]
- Overall Survival (OS) [Time Frame: at 12, 24 and 60 months after start of treatment] [Designated as safety issue: No]

Estimated Enrollment:	652
Study Start Date:	August 2012
Estimated Study Completion Date:	December 2020
Estimated Primary Completion Date:	December 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions

Experimental: Nilotinib+IFN Patients will receive nilotinib 300 mg BID given as two 150 mg capsules twice daily with Peginterferon α2b at a starting target dose of 30µg/week.	Drug: Peginterferon α2b Patients will receive nilotinib 300 mg BID given as two 150 mg capsules twice daily with at a starting target dose of 30µg/week. After confirmed MMR or at least 24 mo. after start of therapy, maintenance therapy (nilotinib will be discontinued) will start for a study duration of up to 5 years. Other Name: Redipen
Active Comparator: Nilotinib Patients will receive nilotinib 300 mg BID given as two 150 mg capsules twice daily.	Drug: Nilotinib Patients will receive nilotinib 300 mg BID given as two 150 mg capsules twice daily for a study duration of up to 5 years. Other Name: Tasigna

Detailed Description:
Objectives

Primary:

- Evaluation of the major molecular response (MMR) rate at 18 months of nilotinib compared to nilotinib+pegylated Interferon alpha (IFN) in adult patients with newly diagnosed Ph/BCR-ABL CML in chronic phase.
- Evaluation of the feasibility to discontinue drug therapy in stable deep molecular response (MR4) after nilotinib versus IFN maintenance therapy.

Secondary:

- Evaluation of the efficacy and tolerability of IFN added to nilotinib 2x300 mg/day.
- Evaluation of the efficacy and tolerability of a maintenance therapy with nilotinib versus IFN after stable MMR after at least 24 months of nilotinib therapy.

Eligibility

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

Criteria
Inclusion Criteria:

- Male or female patients with diagnosis of CP-CML with cytogenetic confirmation of Ph chromosome [t(9;22)(q34;q11)]

- Ph negative cases or patients with variant translocations who are BCR-ABL positive in multiplex PCR (Cross, et al 1994) are eligible as well
- ECOG performance status of < 2
- Pretreatment with hydroxyurea for 6 months and imatinib or nilotinib for a duration of up to 6 weeks is permitted
- Age ≥ 18 years old (no upper age limit given)
- Normal serum levels ≥ LLN (lower limit of normal) of potassium, magnesium, total calcium corrected for serum albumin, or corrected to within normal limits with supplements
- ASAT and ALAT ≤ 2.5 x ULN (upper limit of normal) or ≤ 5.0 x ULN if considered due to leukemia
- Alkaline phosphatase ≤ 2.5 x ULN unless considered due to leukemia
- Total bilirubin ≤ 1.5 x ULN, except known Mb. Gilbert
- Serum lipase and amylase ≤ 1.5 x ULN
- Serum creatinine ≤ 2 x ULN
- Written informed consent prior to any study procedures being performed

Exclusion Criteria:

- Known impaired cardiac function, including any of the following:
  - Left ventricular ejection fraction (LVEF) < 45%
  - Congenital long QT syndrome
  - History of or presence of clinically significant ventricular or atrial tachyarrhythmias
- Clinically significant resting bradycardia (< 50 beats per minute)
- QTc > 450 msec on screening ECG. If QTc > 450 ms and electrolytes are not within normal ranges before nilotinib dosing, electrolytes should be corrected and then the patient rescreened for QTc criterion
- Myocardial infarction within 12 months prior to starting therapy
- Other clinical significant heart disease (e.g. unstable angina, congestive heart failure, uncontrolled hypertension)
- History of acute (i.e., within 1 year of starting study medication) or chronic pancreatitis
- Acute or chronic viral hepatitis with moderate or severe hepatic impairment (Child-Pugh scores > 6), even if controlled
- Other concurrent uncontrolled medical conditions (e.g., uncontrolled diabetes, active or uncontrolled infections, acute or chronic liver and renal disease) that could cause unacceptable safety risks or compromise compliance with the protocol
- Impaired gastrointestinal function or disease that may alter the absorption of study drug (e.g., ulcerative disease, uncontrolled nausea, vomiting and diarrhea, malabsorption syndrome, small bowel resection or gastric by-pass surgery)

- Concomitant medications with potential QT prolongation
- Concomitant medications known to be strong inducers or inhibitors of the CYP450 isoenzyme CYP3A4
- Patients who have undergone major surgery ≤ 2 weeks prior to starting study drug or who have not recovered from side effects of such therapy
- Patients who are pregnant or breast feeding, or women of reproductive potential not employing an effective method of birth control. (Women of childbearing potential must have a negative serum pregnancy test within 14 days prior to administration of nilotinib). Post menopausal women must be amenorrheic for at least 12 months in order to be considered of non-childbearing potential. Female patients must agree to employ an effective barrier method of birth control throughout the study and for up to 3 months following discontinuation of study drug
- Known diagnosis of human immunodeficiency virus (HIV) infection (HIV testing is not mandatory)
- Active autoimmune disorder, including autoimmune hepatitis
- Known serious hypersensitivity reactions to peginterferon alfa-2b or interferon alfa-2b or drug excipients
- Known serious hypersensitivity reactions to nilotinib
- Patients with a history of another primary malignancy that is currently clinically significant or currently requires active intervention
- Patients unwilling or unable to comply with the protocol

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01657604

Contacts

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Show 99 Study Locations

Sponsors and Collaborators

University of Jena

Investigators

Principal Investigator: Andreas Hochhaus, Prof. MD Jena University Hospital

More Information

No publications provided

Responsible Party:	Prof. Dr. med. Andreas Hochhaus, Chair, Dept. Hematology/Oncology, University of Jena
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Keywords provided by University of Jena:
CML
Tasigna
Nilotinib
Interferon

Additional relevant MeSH terms:

Leukemia	Antiviral Agents
Leukemia, Myeloid	Anti-Infective Agents
Leukemia, Myelogenous, Chronic, BCR-ABL Positive	Therapeutic Uses
Neoplasms by Histologic Type	Pharmacologic Actions
Neoplasms	Immunologic Factors
Myeloproliferative Disorders	Physiological Effects of Drugs
Bone Marrow Diseases	Angiogenesis Inhibitors
Hematologic Diseases	Angiogenesis Modulating Agents
Interferon-alpha	Growth Substances
Interferon Alfa-2a	Growth Inhibitors
Interferons	Antineoplastic Agents

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