Trial record **3 of 6** for: Asciminib | CML

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Frontline Asciminib Combination in Chronic Phase CML (CMLXI)

ClinicalTrials.gov Identifier: NCT03906292

Recruitment Status : Recruiting
First Posted : April 8, 2019
Last Update Posted : January 27, 2020

See **Contacts and Locations**

Sponsor:
Thomas Ernst, PD Dr. med.

Collaborators:
Ludwig-Maximilians - University of Munich
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Thomas Ernst, PD Dr. med., University of Jena

Study Description

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Brief Summary:

Adult male and female patients with newly diagnosed Philadelphia chromosome positive (Ph+) and/or BCR-ABL1 positive CML can be included in the study until 3 months after diagnosis. A <4 week pretreatment with hydroxyurea is permitted. Patients treated for <6 weeks with nilotinib 300 mg BID, imatinib 400 mg QD, or dasatinib 100 mg QD are eligible for recruitment and will be allocated to the respective cohort. All patients must provide written informed consent to be enrolled in the trial. Cohorts were designed to allow assessment of QD and BID **asciminib** based combinations to optimize quality of life and compliance. Patients will not be randomized. In general, cohorts will be filled consecutively. **Asciminib** therapy will be commenced 12 weeks after start of nilotinib, imatinib or dasatinib and after recovery of hematopoiesis. Referred patients already treated with imatinib, nilotinib or dasatinib will remain on the initial drug and will be allocated to the respective cohort.

Condition or disease	Intervention/treatment	Phase
Chronic Myeloid Leukemia	Drug: Imatinib Drug: Nilotinib 300 mg Drug: Dasatinib Drug: **Asciminib**	Phase 2

Detailed Description:

Despite the dramatic progress made over the past decade with TKIs in the treatment of CML, allogeneic stem cell transplant remains the only proven curative therapy. To achieve cure or benefit from treatment-free remissions with pharmacologically-based therapies, it is estimated that patients will likely need to achieve a sustained reduction in tumor burden corresponding to a deep molecular response of at least 4 logs (MR4). Currently, only 30.8% of patients achieve a deep molecular response after 12 months of treatment with single agent nilotinib.

The development of the novel and potent BCR-ABL1 allosteric inhibitor, asciminib, presents an opportunity to assess the effect of a different mechanism of inhibition of BCR-ABL1 in the first-line treatment of CML to enhance speed of response and to increase the patient population benefitting from deep molecular response. Dosing a combination of asciminib with an ATP-site inhibitor also has the potential to prevent the emergence of resistance due to point mutations being acquired in one of the binding sites.

The safety, tolerability and pharmacokinetic profile of asciminib as a single agent and in combination

with either nilotinib or imatinib or dasatinib was assessed in a phase-I study. At the doses chosen here, all three combination treatments were well tolerated.

Since in all patient cohorts the standard of care therapy will remain the backbone of initial therapy, there is no reason to expect an efficacy problem with the combination therapies.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	120 participants
Allocation:	Non-Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	4 parallel cohorts
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Frontline **Asciminib** Combination in Chronic Phase **CML**
Actual Study Start Date :	August 19, 2019
Estimated Primary Completion Date :	November 2022
Estimated Study Completion Date :	November 2022

Resource links provided by the National Library of Medicine NIH NLM

Genetics Home Reference related topics: Chronic myeloid leukemia

Drug Information available for: Imatinib Dasatinib

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

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: **Asciminib** 60mg QD Standard therapy of Imatinib 400 mg QD and **asciminib** 60 mg QD	Drug: Imatinib Imatinib 400 mg QD and **asciminib** 60 mg QD Other Name: Imatinib 400 mg QD and **asciminib** 60 mg QD

Arm	Intervention/treatment
	Drug: **Asciminib** **Asciminib**
Experimental: Asciminb 20 mg BID Standard therapy of Nilotinib 300 mg BID and **asciminib** 20 mg BID	Drug: Nilotinib 300 mg Nilotinib 300 mg BID and **asciminib** 20 mg BID or 40 mg QD Other Name: Nilotinib 300 mg BID and **asciminib** 20 mg BID or 40 mg QD Drug: **Asciminib** **Asciminib**
Experimental: **Asciminib** 40 mg QD Standard therapy of Nilotinib 300 mg BID and **asciminib** 40 mg QD	Drug: Nilotinib 300 mg Nilotinib 300 mg BID and **asciminib** 20 mg BID or 40 mg QD Other Name: Nilotinib 300 mg BID and **asciminib** 20 mg BID or 40 mg QD Drug: **Asciminib** **Asciminib**
Experimental: **Asciminib** 80 mg QD Standard therapy of Dasatinib 100 mg QD and **asciminib** 80 mg QD	Drug: Dasatinib Dasatinib 100 mg QD and **asciminib** 80 mg QD Other Name: Dasatinib 100 mg QD and **asciminib** 80 mg QD Drug: **Asciminib** **Asciminib**

Outcome Measures

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Primary Outcome Measures :

1. deep molecular response (Rate of MR4) [Time Frame: at month 12 after Start of Therapy]

   Achievement of deep molecular response (MR4) throught standardized testing of BCR-ABL-transcript Levels

Secondary Outcome Measures :

1. molecular response (MMR and MR4.5) [Time Frame: at and by 6, 12, 18 and 24 months after Start of Therapy]

   Achievement of deep molecular response throught standardized testing of BCR-ABL-transcript levels

2. Adverse Events [Time Frame: at and by baseline, 3, 6, 12, 15, 18, 21 and 24 months after Start of Therapy]

   Incidence of adverse events grade 1-5 and 3-5

3. Progression free survival [Time Frame: at month 24 after Start of Therapy]

   Progression free survival at the end of the study

4. Overall survival [Time Frame: at month 24 after Start of Therapy]

   Overall survival at the end of the study

Eligibility Criteria

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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, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Male or female patients with diagnosis of CP-CML with cytogenetic confirmation of the Ph+ chromosome [t(9;22)(q34;q11)].
- Ph-negative cases or patients with variant translocations who are BCR-ABL1 positive in multiplex PCR 35 will be also considered eligible.
- ECOG performance status of ≤2.
- Age ≥ 18 years old (no upper age limit is given)
- Serum levels of potassium, magnesium, total calcium within the normal limits (≥LLN [lower limit of normal] and ≤ULN [upper limit of normal]). Correction of electrolytes levels with supplements to fulfil enrolment criteria is allowed.
- AST and ALT ≤2.5 x ULN 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 Gilbert disease
- Serum creatinine ≤2 x ULN
- Written informed consent prior to any study procedures being performed.

Exclusion Criteria:

- Allogeneic stem cell transplantation
- Known impaired cardiac function, including any of the following:
  - Congenital long QT syndrome
  - History of or presence of clinically significant ventricular or atrial tachyarrhythmia
  - QTc >450 msec on screening ECG
  - Myocardial infarction within 12 months prior to starting therapy
- Other clinical significant heart disease (e.g. unstable angina, congestive heart failure)
- 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., 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 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 breastfeeding 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 of study start. Post-menopausal women must be amenorrheic for at least 12 months in order to be considered of non-childbearing potential. Male and female patients must agree to employ an effective method of birth control throughout the study and for up to 2 weeks following discontinuation of study drug
- Known diagnosis of human immunodeficiency virus (HIV) infection (HIV testing is not mandatory)
- Known serious hypersensitivity reactions to asciminib, imatinib, nilotinib or dasatinib
- 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

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Information from the National Library of Medicine

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): ***NCT03906292***

Contacts

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Contact: Christian Fabisch, Dr.	+49 3641 ext 9396670	fascination@med.uni-jena.de

Locations

Show 20 study locations

Sponsors and Collaborators

Thomas Ernst, PD Dr. med.

Ludwig-Maximilians - University of Munich

Novartis Pharmaceuticals

Investigators

Principal Investigator: Thomas Ernst, PD Dr. med. University Hospital Jena

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Responsible Party:	Thomas Ernst, PD Dr. med., Principal Investigator, University of Jena
ClinicalTrials.gov Identifier:	NCT03906292 History of Changes
Other Study ID Numbers:	Fascination
	2018-002256-33 (EudraCT Number)
First Posted:	April 8, 2019 Key Record Dates
Last Update Posted:	January 27, 2020
Last Verified:	January 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product:	No
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	No

Additional relevant MeSH terms:

Leukemia, Myelogenous, Chronic, BCR-ABL Positive	Dasatinib
Leukemia, Myeloid, Chronic-Phase	Antineoplastic Agents
Leukemia, Myeloid	Protein Kinase Inhibitors
Leukemia	Enzyme Inhibitors
Neoplasms by Histologic Type	Molecular Mechanisms of Pharmacological Action
Neoplasms	Vitamin B Complex
Myeloproliferative Disorders	Vitamins
Bone Marrow Diseases	Micronutrients
Hematologic Diseases	Nutrients
Niacinamide	Growth Substances
Imatinib Mesylate	Physiological Effects of Drugs