Trial record **1 of 1** for: Naut

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2nd TKI-stop After 2 Years Nilotinib Pre-treatment in Patients With First Unsuccessful Treatment Discontinuation in CML (NAUT)

This study is currently recruiting participants.

See Contacts and Locations

Verified September 2016 by European LeukemiaNet

Sponsor:
European LeukemiaNet

ClinicalTrials.gov Identifier:
NCT02917720

First Posted: September 28, 2016
Last Update Posted: August 24, 2017

Collaborators:
Heidelberg University
Ludwig-Maximilians - University of Munich

Information provided by (Responsible Party):
European LeukemiaNet

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How to Read a Study Record

Purpose

The main goal of the study is the assessment of duration of major molecular response (MMR) or better at 12 and 36 months after stopping tyrosine kinase inhibitors (TKI) therapy a second time in patients with at least three years prior TKI treatment comprising at least two years of nilotinib treatment within this trial and maintained stable MR4 (BCR-ABL ratio <0,01% on international Scale (IS) for at least one year and MR4.5 (BCR-ABL ratio <0,0032% on IS) for at least 6 months:

- who failed a first stop in the EURO-SKI study (standardized criteria)
- who failed a first stop outside the EURO-SKI study but would have had fulfilled same eligible criteria and were stopped according to EURO-SKI rules
- who failed a first stop outside the EURO-SKI study without fulfilling EURO-SKI rules

Condition	Intervention	Phase
Chronic Myeloid Leukemia	Other: TKI discontinuation Drug: nilotinib	Phase 2

Study Type: Interventional

Study Design: Intervention Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Official Title: Multicenter Prospective Trial After First Unsuccessful Treatment Discontinuation in Chronic Myeloid Leukemia (CML) Estimating the Efficacy of Nilotinib in Inducing the Persistence of Molecular Remission After Stopping TKI a 2nd Time

Resource links provided by NLM:

Genetics Home Reference related topics: chronic myeloid leukemia

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Nilotinib

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 European LeukemiaNet:

Primary Outcome Measures:

- Assessment of duration of MMR or better at 12 months after stopping TKI therapy a second time [Time Frame: 12 months after stopping]

  Assessment of duration of MMR or better at 12 months after stopping TKI therapy a second time in patients with at least three years prior TKI treatment comprising at least two years of nilotinib treatment within this trial and maintained stable MR4 for at least one year and MR4.5 for at least 6 months

Secondary Outcome Measures:

- Assessment of quality of life (QoL) profiles under nilotinib treatment and comparison with previous TKI therapy before switch and after stopping [Time Frame: 5 years]

  To investigate QoL changes over time in relapse-free patients without TKI re-start as measured by the EORTC QLQ-C30 and CML 24 (one combined questionnaire)

- Identification of clinical and biological factors correlating with the persistence of MMR or better after stopping TKI [Time Frame: 6 months after stopping]

  Proportion of high risk patients according to the risk score at 6 months after stopping TKI;

- Estimation of overall survival [Time Frame: 3 years]

  Overall survival is calculated from the date of 2nd stop of TKI treatment until the date of death irrespective of the cause of death. Patients still alive at the date of analysis will be censored at the date of last follow-up.

- Time to re-achievement of MR4.5 after restart of therapy [Time Frame: 3 years]

  Assessment of molecular response after 3 years

- Number of patients with grade 1 through grade 5 adverse events (AEs) that are related to study srug, graded according to NCI CTCAE Version 3.0 [Time Frame: 3 years]

  Assessment of incidence of any AEs (e.g. from musculoskeletal system) that arise after stopping TKI treatment a second time

- Assessment of duration of MMR or better [Time Frame: 36 months after stopping]

  Assessment of duration of MMR or better at 36 months after stopping TKI therapy a second time in patients with at least three years prior TKI treatment comprising at least two years of nilotinib treatment

- Number of patients with grade 1 through grade 5 adverse events (AEs) that are related to study srug, graded according to NCI CTCAE Version 3.0 [Time Frame: 2 years treatment with nilotinib 300 mg/bid]

  Assessment of incidence of any AEs (e.g. from musculoskeletal system) that arise after stopping TKI treatment a second time

- Estimation of progression-free survival [Time Frame: 3 years]

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

- Identification of clinical and biological factors correlating with the persistence of MMR or better after 6 months [Time Frame: 6 months after stopping]

  Proportion of female patients without molecular relapse

Estimated Enrollment:	200
Study Start Date:	December 2016
Estimated Study Completion Date:	May 2023
Estimated Primary Completion Date:	May 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: TKI-stop, pre-treatment with nilotinib Treatment after unsuccessful 1st discontinuation at least two year with nilotinib (300 mg/bid). In total, retreatment with TKI for at least 3 years before entering screening for stopping phase is warranted. Clinical monitoring every 3 months during this 2 years. Patients who re-achieved and maintained MR4 for at least 12 months and MR4.5 for at least 6 months can enter screening phase for TFR .If MR4.5 is confirmed by an validated laboratory, patient may enter stopping phase of the study. Patient not fulfilling these criteria can be screened again every 3 months until month 48. After TKI-stop hematological monitoring and quantitative PCR of BCR/ABL1 (month 1-6 after stopping: monthly; month 7-12 after stopping: every 1.5 months, thereafter once every three months, for 3 years in total.	Other: TKI discontinuation 2nd TKI stop after pre-treatment with nilotinib. Drug: nilotinib Pre-treatment with nilotinib 300 mg/bid for 2 years

Relapse is defined as BCR-ABL1 > 0.1% on IS at a single time point (loss of MMR) In case of relapse restart of TKI. In general, the same TKI (nilotinib) as before second stop is recommended	

Detailed Description:

The proposal is to re-treat patients with a minimum of two years with nilotinib 2x300 mg/d resulting in total of at least three years TKI treatment who show recurrent disease after unsuccessful first stop after TKI treatment in or outside the EURO-SKI study.

If MR4 or better is re-achieved and maintained for at least one year and MR4.5 or better is re-achieved and maintained for at least 6 months, patients will be eligible for a second stop attempt within this study. For MR4, three consecutive PCRs with MR4 or deeper should be measured within one year and for MR4.5, two PCRs during 6 months should demonstrate a MR4.5.

Patients who exhibited hematological relapse after the first stop attempt will not be eligible for a second stop attempt within this study.

After inclusion, 3 monthly monitoring will be performed under nilotinib treatment within the trial. Patients fulfilling the criteria mentioned above will then enter the screening phase.

After verification of MR4.5, TKI treatment will be stopped and patients followed in the same manner as described in EURO-SKI (monthly PCRs for 6 months, 6-weekly PCRs 7-12 months after stopping, thereafter 3-monthly). If MMR is lost (BCR-ABL >0.1% (IS)), TKI treatment will once again be restarted; here the same TKI (nilotinib) is recommended.

It is assumed that after failure of first stop a switch to treatment with 2GTKI may increase the chance of stopping a second time [Legros et al. Blood 2012; Rea et al. Blood 2014] It is expected that the rate of a successful second stop at 12 and 36 months is more than 25%.

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Age ≥ 18 years
- Patients with Ph chromosome and/or the BCR-ABL (either b3a2 and /or b2a2) fusion gene positive CML
- CML in CP having failed a prior attempt to stop imatinib or other TKIs therapy either within EURO-SKI or not
- Pretreatment at least one year with any TKI after 1st stop
- Written informed consent

Exclusion Criteria:

- Previous hematological relapse after first stop of TKI.
- Failure to any TKI at any time during CML treatment according to current ELN criteria
- Previous planned or performed allo SCT
- Previous AP/BC at any time in the history of the disease
- High cardiac risk according to ESC score
- Impaired cardiac function including any of the following:
- Use of a ventricular paced pacemaker; congenital long QT syndrome or family history of; history or presence of significant ventricular or atrial tachyarrhythmias; clinically significant resting bradycardia (<50 bpm); QTcF >450 msec at baseline, myocardial infarction before baseline; other clinically significant heart disease (e.g., unstable angina, congestive heart failure, or uncontrolled hypertension).
- Treatment with inhibitors of CYP3A4 or medications that have been well documented to prolong the QT interval is contraindicated.
- History of acute pancreatitis within one year of study entry or medical history of chronic pancreatitis.
- Any other malignancy except if neither clinically significant nor requires active intervention.
- Severe or uncontrolled medical conditions (i.e., uncontrolled diabetes, acute or chronic liver disease, pancreatic, or severe renal disease unrelated to tumor, active or uncontrolled infection).
- Women who are pregnant, breast feeding, or of childbearing potential without a negative serum pregnancy test at baseline. Male or female patients of childbearing potential unwilling to use an effective barrier contraceptive method

Contacts and Locations

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): ***NCT02917720***

Contacts

Contact: Susanne Saußele, PD Dr. med. +49 621 383 ext 6966 susanne.saussele@medma.u

Locations

Germany

Universitätsklinikum der RWTH Aachen, Germany, 52074 Contact: Tim H. Brümmendorf, Dr. med.	**Recruiting**
Klinikum Bayreuth Bayreuth, Germany, 95445 Contact: Alexander Kiani, Dr. med.	**Recruiting**
Vivantes Klinikum Neukölln Berlin, Germany, 12351 Contact: Maike de Wit, Dr. med.	**Not yet recruiting**
Klinikum Chemnitz Chemnitz, Germany, 09113 Contact: Mathias Hänel, Dr. med.	**Recruiting**
Onkologische Schwerpunktpraxis Esslingen, Germany, 73728 Contact: Robert Eckert, Dr. med.	**Not yet recruiting**
Centrum für Hämatologie und Onkologie Bethanien Frankfurt, Germany, 60389 Contact: Hans Tesch, Dr. med.	**Recruiting**
Schwerpunktpraxis Onkologie Heilbronn, Germany, 74072 Contact: Jolanta Dengler, Dr. med.	**Recruiting**
	Recruiting

Universitätsklinikum Jena
Jena, Germany, 07740
Contact: Andreas Hochhaus

Sponsors and Collaborators

European LeukemiaNet

Heidelberg University

Ludwig-Maximilians - University of Munich

Investigators

Principal Investigator: Norbert Huber, Dr. Heidelberg University

More Information

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Plan to Share IPD: No

Keywords provided by European LeukemiaNet:
TKI discontinuation

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