PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

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

Trial Acronym

TIGER

URL of the trial

[---]*

Brief Summary in Lay Language

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.

Brief Summary in Scientific Language

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.

Organizational Data

- DRKS-ID: **DRKS00005243**
- Date of Registration in DRKS: **2013/10/18**
- Date of Registration in Partner Registry or other Primary Registry: **2012/07/09**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- EudraCT-No.
  (for studies acc. to Drug Law): **2010-024262-22**
- Primary Registry-ID: **NCT01657604 (ClinicalTrials.gov)**
- Sponsor-ID: **CML V (University of Jena)**
- Other Secondary-ID: **2010-024262-22**

Health condition or Problem studied

- Free text: **Chronic Myeloid Leukemia**
- ICD10: **C92.1 - Chronic myeloid leukaemia**

Interventions/Observational Groups

- Arm 1: **Drug: Peginterferon α2b**
- Arm 2: **Drug: Nilotinib**

Characteristics

- Study Type: **Interventional**

Study Type: **Interventional**

- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Diagnostic**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- MMR rate at 18 months of nilotinib monotherapy versus nilotinib+pegylated interferon alpha; time frame: at least 18 months after start of study treatment; 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; rate of patients with molecular relapse (loss of MMR) 12 months after discontinuation of any treatment for CML

Secondary Outcome

- rate of CCyR and MMR; time frame: at 12, 18 and 24 months after start of treatment
- 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); 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)
- Progression-Free Survival (PFS); time frame: at 12, 24 and 60 months after start of treatment
- Rate of patients off treatment for at least 6 months; time frame: at 60 months after start of treatment; 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); 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)
- 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)
- pharmacoeconomics of the treatment strategies; time frame: after end of study

(expected in December 2020) (up to 8 years)
- Overall Survival (OS); time frame: at 12, 24 and 60 months after start of treatment

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- **Universitätsklinikum Aachen Medizinische Klinik IV, Aachen**
- **Gesundheitszentrum St. Marien GmbH, Onkologie/ Hämatologie Onkologisches Zentrum, Amberg**
- **MVZ am Klinikum Arnsberg GmbH, Hämatologie - Internistische Onkologie, Arnsberg**
- **Helios Klinikum Bad Saarow, Klinik für Hämatologie, Onkologie und Palliativmedizin, Bad Saarow**
- **Klinikum Bayreuth GmbH, Bayreuth**
- **Charité - Campus Benjamin Franklin Medizinische Klinik III, Berlin**
- **Charité CVK, CC14, Klinik für Hämatologie und Onkologie, Berlin**
- **Vivantes Netzwerk für Gesundheit GmbH, Klinikum Neukölln, Klinik für Innere Medizin - Hämatologie und Onkologie, Berlin**
- **Universitätsklinikum Bonn Med. Klinik und Poliklinik III, Hämatologie, Bonn**
- **Evangelische Kliniken Bonn gGmbH Johanniterkrankenhaus, Bonn**
- **Städtisches Klinikum Braunschweig gGmbh, Medizinische Klinik III - Hämatologie, Braunschweig**
- **DIAKO Ev. Diakonie-Krankenhaus gGmbH, Medizinische Klinik II, Bremen**
- **Klinikum Bremen-Mitte gGmbH, Bremen**
- **Klinikum Chemnitz gGmbH Klinik für Innere Medizin III, Chemnitz**
- **Praxis Dr. med. Zöller, Coburg**
- **Onkologische Schwerpunktpraxis, Cottbus**
- **Onkologische Schwerpunktpraxis, Dresden**
- **Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden, Dresden**
- **Gemeinschaftspraxis Mohm / Prange-Krex, Dresden**
- **Marien Hospital Düsseldorf; Klinik für Onkologie, Hämatologie und Palliativmedizin, Düsseldorf**
- **Onkologisch-Hämatologische Schwerpunktpraxis, Eisenach**

- **Universitätsklinikum Erlangen Medizinische Klinik 5 - Hämatologie und int. Onkologie, Erlangen**
- **Onkologische Schwerpunktpraxis Erlangen, Onkologie, Hämatologie, Erlangen**
- **St.-Antonius-Hospital, Klinik für Hämatologie Onkologie, Eschweiler**
- **Klinik für Hämatologie Universitätsklinikum Essen, Essen**
- **Universitätsklinikum Freiburg Abteilung Innere Medizin I - Hämatologie und Onkologie, Freiburg**
- **MVZ-Osthessen GmbH Klinikum Fulda Tumorklinik, Fulda**
- **Praxis Dr. med. Schmitt, Gerlingen**
- **Wilhelm-Anton-Hospital gGmbH, Klinik für Innere Medizin, Hämatologie und Internsitische Onkologie, Goch**
- **Dr. med. Hans Werner Tessen, Facharzt für Innere Medizin, Goslar**
- **Universitätsmedizin Greifswald, Klinik und Poliklinik für Innere, Greifswald**
- **Georg-August Universität Göttingen Abteilung Hämatologie und Onkologie, Göttingen**
- **Internistische Gemeinschaftspraxis, Güstrow**
- **Katholisches Krankenhaus Hagen gem. GmbH, Klinik für Hämatologie und, Hagen**
- **Gemeinschaftspraxis Hämatologie und internistische, Halle**
- **Asklepios Klinik St. Georg, Abteilung Hämatologie, Onkologie, Stammzelltransplantation, Hamburg**
- **Hämatologisch-Onkologische Praxis Altona, Struensee-Haus, Hamburg**
- **Universitätsklinikum Hamburg- Eppendorf, Medizinische Klinik 2, Hamburg**
- **St. Marien-Hospital Hamm Klinik für Hämatologie und Onkologie, Hamm**
- **Evangelisches Krankenhaus Hamm, Hamm**
- **Medizinische Hochschule Hannover, Klinik für Hämatologie, Hämostaseologie, Onkologie und Stammzelltransplantation, Hannover**
- **Mediprojekt, Gesellschaft für Medizinstatistik und Projektentwicklung, Hannover**
- **Universitätsklinikum Heidelberg Innere Medizin V: Hämatologie, Onkologie und Rheumatologie, Heidelberg**
- **Internistische Gemeinschaftspraxis Heilbronn, Heilbronn**
- **St. Bernward Krankenhaus Hildesheim, Hildesheim**
- **Universitätsklinikum des Saarlandes Klinik für Innere Medizin I, Homburg/ Saar**
- **Klinikum Idar-Oberstein GmbH, Innere Medizin I (Hämatologie/Onkologie), Idar-Oberstein**
- **MVZ Onkologie Ingolstadt, Ingolstadt**

- **Universitätsklinikum Jena, Klinik für Innere Medizin II, Abt. Hämatologie und internistische Onkologie, Jena**
- **Eps- early phase solutions GmbH, Jena**
- **Westpfalz-Klinikum GmbH Innere 1, Kaiserslautern**
- **St. Vincentius-Kliniken Karlsruhe, Karlsruhe**
- **Städtisches Klinikum Karlsruhe gGmbH, Medizinische Klinik III: Hämatologie/Onkologie, Karlsruhe**
- **Universitätsklinikum Schleswig-Holstein, II. Medizinische Klinik und Poliklinik im Städtischen Krankenhaus Kiel, Kiel**
- **InVO, Institut für Versorgungsforschung in der Onkologie, Koblenz**
- **Onkologische Gemeinschaftspraxis Dr. M. Neise u. Dr. A. Lollert, Krefeld**
- **Onkologische Schwerpunktpraxis, Kronach**
- **Hämatologisch-Onkologische Tagesklinik, Landshut**
- **Onkologisches Zentrum Gemeinschaftspraxis für Hämato-/ Onkologie, Abt. für Hämato-/ Onkologie im Caritas Krankenhaus, Lebach**
- **Onkologisches Schwerpunktpraxis, Leer**
- **Universitätsklinikum Leipzig, Department für Innere Medizin, Leipzig**
- **Dr. Aldaoud - Dr. Schwarzer Forschungsgesellschaft mbH, Leipzig**
- **Krankenhausgesellschaft St. Vincenz mbH Limburg, Limburg/Lahn**
- **Gemeinschaftspraxis Uhle, Müller, Kröning, Jentsch-Ullrich, Magdeburg**
- **Universitätsmedizin der Johannes- Gutenberg Universität Mainz, III. Medizinische Klinik und Poliklinik, Hämatologie, internistische Onkologie und Pneumologie, Mainz**
- **Internistische Gemeinschaftspraxis Onkologie/Hämatologie, Mainz**
- **Mannheimer Onkologie Praxis, Mannheim**
- **Universitätsmedizin Mannheim III. Medizinische Klinik, Mannheim**
- **Klinikum der Philipps-Universität Marburg, Klinik für Innere Medizin, Schwerpunkt Hämatologie, Onkologie und Immunologie, Marburg**
- **Johannes Wesling Klinikum Minden, Mühlenkreiskliniken (AöR), Hämatologie/Onkologie, Minden**
- **Stauferklinikum Schwäbisch Gmünd, Zentrum Innere Medizin, Mutlangen**
- **Gemeinschaftspraxis Hämatologie/ Onkologie, München**
- **Klinikum rechts der Isar, III. Medizinische Klinik und Poliklinik, München**
- **MHP Münchener Hämatologie Praxis, München**
- **Hämatologisch-Onkologische Schwerpunktpraxis, München**
- **Tumorzentrum München Süd, Klinikum Hanaching, München**

- **Hämatologisch-Onkologische Gemeinschaftspraxis, München**
- **Universitätsklinikum Grosshadern LMU München, München**
- **Onkologische und hämatologische Schwerpunktpraxis, Neumarkt**
- **Ambulantes BehandlungsCentrum des Klinikums Nürnberg, Hämatologie/Onkologie, Nuklearmedizin, Nürnberg**
- **Klinikum Oldenburg Klinik für Onkologie und Hämatologie / Innere Medizin II, Oldenburg**
- **Klinikum Passau, II. Medizinische Klinik, Passau**
- **Klinikum Vest, Behandlungszentrum Recklinghausen, Medizinische Klinik III, Recklinghausen**
- **Universitätsklinikum Regensburg Abteilung für Hämatologie und internistische Onkologie, Regensburg**
- **Krankenhaus Barmherzige Brüder Regensburg, Klinik für Onkologie und Hämatologie, Regensburg**
- **Kreiskliniken Reutlingen GmbH, Klinikum am Steinenberg, Medizinische Klinik I, Reutlingen**
- **Universitätsmedizin Rostock, ZIM II Klinik für Hämatologie, Onkologie und, Rostock**
- **Leopoldina-Krankenhaus, Schweinfurt**
- **Diakonie-Klinikum Schwäbisch Hall gGmbH, Innere Medizin III: Sektion für Onkologie und Hämatologie, Schwäbisch Hall**
- **Klinikverbund Südwest, Kliniken Sindelfingen-Böblingen gGmbH, Sindelfingen**
- **Diakonie Klinikum Stuttgart, Medizinische Klinik, Stuttgart**
- **Klinikum Mutterhaus der Borromäerinnen, Trier**
- **Medizinische Universitätsklinik, Department für Innere Medizin GCP Studienzentrale der Abteilung 2, Tübingen**
- **Universitätsklinikum Ulm Klinik für Innere Medizin III, Ulm**
- **Schwarzwald-Baar Klinikum Villingen-Schwenningen GmbH, Villingen-Schwenningen**
- **Medizinisches Versorgungszentrum GmbH, Weiden**
- **Dres. med. T. Kamp - R. Eckert Innere/Hämatologie/Onkologie, Wendlingen**
- **Onkologische Gemeinschaftspraxis Würselen und Stolberg, Würselen**
- **Universitätsklinikum Würzburg Medizinische Klinik und Poliklinik II, Würzburg**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2012/08/31**
- Target Sample Size: **652**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional 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

Addresses

■ **Primary Sponsor**

University of Jena

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

■ **Contact for Scientific Queries**

Jena University Hospital
Andreas Hochhaus, Prof. MD

Telephone: **[---]***
Fax: **[---]***
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Contact for Public Queries

Andreas Hochhaus, Prof. MD

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E-mail: **Andreas.Hochhaus at med.uni-jena.de**
URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 6
- Last processed date by ClinicalTrials.gov: 2013/10/30

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*