# *KURZPROTOKOLL*
# *CAMN107EDE13T (TIGER)*

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| **Öffentlicher Titel** | Behandlungsoptimierung bei Ph positiver CP-CML mit Nilotinib und IFNalpha |
| **Wissenschaftl. Titel** | 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 |
| **Kurztitel** | CAMN107EDE13T (TIGER) |
| **Studienart** | multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig |
| **Studienphase** | Phase III |
| **Erkrankung** | Blut: Myeloische Neoplasien/Dysplasien: Chronische myeloische Leukämie (CML) |

**Einschlusskriterien**

- The investigator or his/her designee must ensure that all patients who meet the following inclusion and exclusion criteria are offered enrolment in the study. Patients must meet all inclusion criteria within 2 weeks of enrolment (bone marrow examinations may be within 12 weeks) and none of the exclusion criteria to enter the study. The investigative site must have all documentation of eligibility on file at the investigative site for confirmation by study monitors.
- 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, 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.

**Ausschlusskriterien**

- 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. Male and female patients must agree to employ an effective 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.

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| **Alter** | 18 Jahre und älter |
| **Molekularer Marker** | BCR-ABL1 |
| **Fallzahl** | 652 |
| **Sponsor** | Universitätsklinikum Jena (Hauptsponsor) |
| **Förderer** | Novartis Pharma |
| **Registrierung in anderen Studienregistern** | ClinicalTrials.gov NCT01657604 (primäres Register)<br>EudraCT 2010-024262-22 |