KURZPROTOKOLL
CAMN107I2201

Öffentlicher Titel	Absetzen von Nilotinib bei CML
Wissenschaftl. Titel	A Single-arm, Multicenter, Nilotinib Treatment-free Remission Study in Patients With BCR-ABL1 Positive Chronic Myelogenous Leukemia in Chronic Phase Who Have Achieved Durable Minimal Residual Disease (MRD) Status on First Line Nilotinib Treatment
Kurztitel	CAMN107I2201
Studienart	multizentrisch, prospektiv, offen/unverblindet, einarmig, Pharma-Studie
Studienphase	Phase II
Erkrankung	Blut: Myeloische Neoplasien/Dysplasien: Chronische myeloische Leukämie (CML)
Einschlusskriterien	- Male or female patients >= 18 years of age - Minimum of 2 calendar years of nilotinib treatment (300 mg BID or transiently lower dose of nilotinib from the perspective of tolerance) for BCR-ABL positive CML in documented chronic phase at the time of diagnosis - Documented chronic phase CML must meet all the criteria defined by: < 15% blasts in peripheral blood and bone marrow; < 30% blasts plus promyelocytes in peripheral blood and bone marrow; < 20% basophils in the peripheral blood; >= 100 x 10^9/L (>= 100,000/mm3) platelets; No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly. - Patients must tolerate a minimum total daily dose of nilotinib of 400mg - Evidence of typical BCR-ABL transcripts (b3a2 or b2a2) at the time of CML diagnosis i.e. prior to first start of TKI treatment which are amenable to standardized RT-PCR quantification” - Patient in MR4.5 at prescreening at Novartis designated lab - ECOG performance status of 0-2 - Adequate end organ function as defined by: Direct bilirubin <= 1.5 x ULN; SGOT(AST) and SGPT(ALT) <= 3 x ULN i.e. equivalent to <= Grade 1 NCI-CTCAE; Serum lipase <= 2 x ULN i.e. equivalent to <= Grade 2 NCI-CTCAE;Alkaline phosphatase <= 2.5 x ULN; Serum creatinine < 1.5 x ULN - Patients must have the following electrolyte values within normal limits or corrected to be within normal limits with supplements prior to first dose of study medication: Potassium (suggested keep to prevent issues with QT and/or rhythm abnormalities); Magnesium (suggested keep to prevent issues with QT and/or rhythm abnormalities); Total calcium (corrected for serum albumin) - Patients must have normal marrow function as defined: Absolute Neutrophil Count (ANC) >= 1.5 x 10^9/L; Hemoglobin >= 9.0 g/dL; Platelets >= 100 x 10^9/L 11. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests and other study procedures - Written informed consent must be obtained prior to any screening procedures.
Ausschlusskriterien	- Previous treatment with BCR-ABL inhibitors other than nilotinib for more than a total cumulative duration of 4 weeks - Previous treatment with alpha-interferon of any duration - Previous anticancer agents for CML other than nilotinib except for cytoreduction after CML diagnosis until up to 4 weeks after first dose of nilotinib - Known second chronic phase of CML after previous progression to AP/BC - Poorly controlled diabetes mellitus (defined as HbA1c > 9%)

- Impaired cardiac function including any one of the following: LVEF < 45% or below the institutional lower limit of the normal range (whichever is higher); Inability to determine the QT interval on ECG; Complete left bundle branch block; Right bundle branch block plus left anterior or posterior hemiblock; Use of a ventricular-paced pacemaker; Congenital long QT syndrome or a known family history of long QT syndrome; History of or presence of clinically significant ventricular or atrial tachyarrhythmias; Clinically significant resting bradycardia; QTc > 450 msec on the average of three serial baseline ECG (using the QTcF formula). If QTcF > 450 msec and electrolytes are not within normal ranges, electrolytes should be corrected and then the patient re-tested for QTc; History or clinical signs of myocardial infarction within 1 year of study entry; History of unstable angina within 1 year of study entry; Other clinically significant heart disease (e.g. congestive heart failure, cardiomyopathy or uncontrolled hypertension)
- Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol (e.g. uncontrolled diabetes, uncontrolled infection)
- History of acute pancreatitis within 1 year of study entry or past medical history of chronic pancreatitis
- Known presence of significant congenital or acquired bleeding disorder unrelated to cancer
- History of another active malignancy within 5 years prior to study entry with the exception of previous or concomitant basal cell skin cancer and previous carcinoma in situ treated curatively
- Patients who have not recovered from prior surgery
- Treatment with other investigational agents (defined as not used in accordance with the approved indication) within 4 weeks of Day 1
- Patients actively receiving therapy with strong CYP3A4 inhibitors and/or inducers, and the treatment cannot be either discontinued or switched to a different medication prior to starting study drug. See Appendix 1 for a list of these medications. This list may not be exhaustive.
- Patients actively receiving therapy with herbal medicines that are strong CYP3A4 inhibitors and/or inducers, and the treatment cannot be either discontinued or switched to a different medication prior to starting study drug. These herbal medicines may include Echinacea, (including E. purpurea, E. angustifolia and E. pallida), Piperine, Artemisinin, St. John’s Wort, and Ginkgo.
- Patients who are currently receiving treatment with any medications that have the potential to prolong the QT interval and the treatment cannot be either safely discontinued or switched to a different medication prior to starting study drug. (Please see http://www.torsades.org/medical-pros/drug-lists/printable-drug-list.cfm for a list of agents that prolong the QT interval)
- Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug (e.g. ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection, or gastric bypass surgery)
- Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.

- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during the study and for 30 days after the final dose of nilotinib. Highly effective contraception is defined as either: Total abstinence (when this is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods); Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment; Male sterilization (at least 6 months prior to enrolling). For female patients on the study the vasectomized male partner should be the sole partner for that patient; Use of a combination of any two of the following: a. Use of oral, injected or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception; b. Placement of an intrauterine device (IUD) or intrauterine system (IUS); c. Barrier methods of contraception: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository In case of use of oral contraception women should have been stable on the same pill for a minimum of 3 months before taking study treatment Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks prior to enrolling. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential. If a study patient becomes pregnant or suspects being pregnant during the study or within 30 days after the final dose of nilotinib, the Study Doctor needs to be informed immediately and ongoing study treatment with nilotinib has to be stopped immediately.

Alter	18 Jahre und älter
Molekularer Marker	BCR-ABL1
Prüfzentren	**Universitätsmedizin Frankfurt** (Rekrutierung beendet) Medizinische Klinik II, Hämatologie/Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Anja Binckebanck Tel: 069 6301-6221 Fax: 069 6301-7463 binckebanck@em.uni-frankfurt.de
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