

KURZPROTOKOLL **CAMN107YDE19**

Öffentlicher Titel	Phase Ib Studie zur kombinierten Therapie mit Nilotinib und Ruxolitinib bei CML oder PH+ALL Patienten
Wissenschaftl. Titel	A Phase Ib single-arm, open-label, multicenter study to assess the safety and tolerability of combined treatment with nilotinib 300mg BID and ruxolitinib increasing dose in CML patients in CP and in AP/BC or relapsed/refractory Ph+ ALL
Kurztitel	CAMN107YDE19
Studienart	multizentrisch, prospektiv, offen/unverblindet, einarmig, Pharma-Studie
Studienphase	Phase I
Erkrankung	Blut: Myeloische Neoplasien/Dysplasien: Chronische myeloische Leukämie (CML) Blut: Akute lymphatische Leukämie (ALL): Rezidiert/refraktär
Ziele	<ul style="list-style-type: none">- Occurrence of dose limiting toxicities (DLTs) [Time Frame: Baseline, up to day 28 (equals first cycle)] [Designated as safety issue: Yes] Occurrence of DLTs during cycle 1- Safety and tolerability profile of nilotinib and ruxolitinib administered in combination [Time Frame: Baseline, up to month 12] [Designated as safety issue: Yes] Maximum Tolerated Dose (MTD) and/or Recommended Phase II Dose (RPIID) of ruxolitinib in combination with nilotinib. (timeframe, baseline up to month 12)- Trough levels of nilotinib and ruxolitinib administered in combination [Time Frame: Baseline, up to month 12] [Designated as safety issue: Yes] Trough levels will be determined by measuring the minimum plasma concentration (Cmin).- Clinical activity of nilotinib and ruxolitinib administered in combination [Time Frame: Baseline and at 3, 6, and 12 months] [Designated as safety issue: No] Chronic myeloid leukemia in chronic phase: assessment of molecular response: MMR ($\leq 0.1\%$ BCR-ABL) and MR4 ($\leq 0.001\%$ BCR-ABL) at 3, 6, 12 months; Advanced disease: assessment of cytogenetic response will be based on evaluating percentage of Ph+ metaphases
Einschlusskriterien	<ul style="list-style-type: none">- Patients of the first stratum must have chronic myeloid leukemia receiving nilotinib first-line therapy or receiving second-line or subsequent-line treatment with nilotinib.- Patients of the second stratum must have CML in AP/BC or relapsed/refractory Ph+ ALL, or be Ph+ ALL patients with MRD with or without prior nilotinib pretreatment;- Patients must have adequate end organ function, as defined by:<ul style="list-style-type: none">- Creatinine $< 2.0 \times$ upper limit of normal (ULN)- Total bilirubin $< 1.5 \times$ ULN ($< 3.0 \times$ ULN if related to disease or polymorphism, such as Mb. Gilbert)- ALT and AST $< 2.5 \times$ ULN ($< 5.0 \times$ ULN if related to disease)- Serum lipase $\leq 1.5 \times$ ULN- Alkaline phosphatase $\leq 2.5 \times$ ULN ($< 5.0 \times$ ULN if related to disease)- Patients must have the following electrolyte values within normal limits or corrected to within normal limits with supplements prior to the first dose of study medication: Potassium, Magnesium, Phosphate, Total calcium (corrected for serum albumin)- Female patients of childbearing potential (WOCBP) must have a negative serum pregnancy test within 7 days before initiation of study drug. All WOCBP must use highly effective contraceptive methods throughout and during 3 months after study;- Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 1 for patients in CP, ≤ 2 for patients in AP/BC or with relapsed/refractory Ph+ ALL or with Ph+ ALL with MRD;- Patient has the following laboratory values within 7 days of starting study drug:<ul style="list-style-type: none">- For CML and Ph+ ALL patients: platelet count $> 75 \times 10^9/L$ and ANC $> 1.0 \times 10^9/L$
Ausschlusskriterien	<ul style="list-style-type: none">- Patient must not have evidence of active malignancy other than the existing CML or ALL

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- Patient must not receive drugs that interfere with coagulation or inhibits platelet function, with the exception of aspirin \leq 150 mg per day or low molecular weight heparin.
- Patient must not have history of platelet dysfunction, bleeding diathesis, and/or coagulopathy in the 6 months prior to screening;
- Patient must not require treatment with any strong CYP3A4 inducer or inhibitor
- Patient must not have history of hypersensitivity to any of the study drugs or to drugs of similar chemical classes and their excipients;
- Patients must not take other investigational drugs within 28 days prior to screening;
- Patient must not be pregnant or lactating at screening and/or baseline;
- Patient must not have impaired cardiac functions
- Other protocol-defined inclusion/exclusion criteria may apply

Alter	18 Jahre und älter
Molekularer Marker	BCR-ABL1
Fallzahl	80
Prüfzentren	Universitätsklinikum 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
Sponsor	Novartis Pharma
Förderer	Novartis Pharma
Registrierung in anderen Studienregistern	EudraCT 2014-000831-18 ClinicalTrials.gov NCT02253277