

## **KURZPROTOKOLL** **CAMN107YDE19**

<b>Öffentlicher Titel</b>	Phase Ib Studie zur kombinierten Therapie mit Nilotinib und Ruxolitinib bei CML oder PH+ALL Patienten
<b>Wissenschaftl. Titel</b>	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
<b>Kurztitel</b>	CAMN107YDE19
<b>Studienart</b>	multizentrisch, prospektiv, offen/unverblindet, einarmig, Pharma-Studie
<b>Studienphase</b>	Phase I
<b>Erkrankung</b>	Blut: Myeloische Neoplasien/Dysplasien: Chronische myeloische Leukämie (CML) Blut: Akute lymphatische Leukämie (ALL): Rezidiert/refraktär
<b>Ziele</b>	<ul style="list-style-type: none"><li>- 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</li><li>- 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)</li><li>- 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).</li><li>- 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 (<math>\leq 0.1\%</math> BCR-ABL) and MR4 (<math>\leq 0.001\%</math> BCR-ABL) at 3, 6, 12 months; Advanced disease: assessment of cytogenetic response will be based on evaluating percentage of Ph+ metaphases</li></ul>
<b>Einschlusskriterien</b>	<ul style="list-style-type: none"><li>- 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.</li><li>- 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;</li><li>- Patients must have adequate end organ function, as defined by:<ul style="list-style-type: none"><li>- Creatinine <math>&lt; 2.0 \times</math> upper limit of normal (ULN)</li><li>- Total bilirubin <math>&lt; 1.5 \times</math> ULN (<math>&lt; 3.0 \times</math> ULN if related to disease or polymorphism, such as Mb. Gilbert)</li><li>- ALT and AST <math>&lt; 2.5 \times</math> ULN (<math>&lt; 5.0 \times</math> ULN if related to disease)</li><li>- Serum lipase <math>\leq 1.5 \times</math> ULN</li><li>- Alkaline phosphatase <math>\leq 2.5 \times</math> ULN (<math>&lt; 5.0 \times</math> ULN if related to disease)</li></ul></li><li>- 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)</li><li>- 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;</li><li>- Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 1 for patients in CP, <math>\leq 2</math> for patients in AP/BC or with relapsed/refractory Ph+ ALL or with Ph+ ALL with MRD;</li><li>- Patient has the following laboratory values within 7 days of starting study drug:<ul style="list-style-type: none"><li>- For CML and Ph+ ALL patients: platelet count <math>&gt; 75 \times 10^9/L</math> and ANC <math>&gt; 1.0 \times 10^9/L</math></li></ul></li></ul>
<b>Ausschlusskriterien</b>	<ul style="list-style-type: none"><li>- Patient must not have evidence of active malignancy other than the existing CML or ALL</li></ul>

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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

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