KURZPROTOKOLL
CABL001X2101

Öffentlicher Titel	Phase I Studie zur Behandlung von CML oder Ph+ALL mit ABL001
Wissenschaftl. Titel	A phase I, multicenter, open-label study of oral ABL001 in patients with chronic myelogenous leukemia or Philadelphia Chromosome-positive acute lymphoblastic leukemia
Kurztitel	CABL001X2101
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig
Studienphase	Phase I
Erkrankung	Blut: Myeloische Neoplasien/Dysplasien: Chronische myeloische Leukämie (CML) Blut: Akute lymphatische Leukämie (ALL): Rezidiviert/refraktär

Einschlusskriterien

- Male or female patients >= 18 years of age who present with the following: a) Patients with Philadelphia chromosome-positive CML in chronic or acceleratedphase who were previously treated with two different tyrosine kinase inhibitors prior to study entry and are relapsed, refractory to or intolerant of TKIs as determined by investigators. There is no restriction on the number of prior therapies administered to patients, and patients who are status post bone marrow transplant are eligible provided they meet the inclusion/exclusion criteria for entry onto the study. Patients with CML in blast crisis are excluded from entry onto this study. Documented blast crisis phase CML will meet all the criteria defined by: >= 30% blasts in peripheral blood or bone marrow aspirate
- Appearance of extramedullary involvement other than hepatosplenomegaly proven by biopsy (i.e., chloroma): a) Patients with Ph+ ALL must have a cytopathologically confirmed diagnosis of Ph+ ALL and be relapsed or refractory to one prior TKI or intolerant of TKIs. TKI failure for Ph+ ALL patients is defined as at least the loss of Molecular Response (MR) 4.5 (BCR-ABL <= 0.0032%); Ph+ ALL patients with stable central nervous system (CNS) disease are eligible to participate and may be treated concurrently with intrathecal (or intra Ommaya) chemotherapy.
- Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2
- Willingness and ability to comply with all study procedures
- Written informed consent obtained prior to any screening procedures

Ausschlusskriterien

- Systemic antineoplastic therapy (including alfa-interferon, unconjugated therapeutic antibodies and toxin immunoconjugates) or any experimental therapy within 14 days or 5 half-lives, whichever is longer, before the first dose of ABL001
- Radiotherapy with a wide field of radiation within 4 weeks or radiotherapy with a limited field of radiation for palliation within 1 week of the first dose of ABL001
- CNS irradiation for meningeal leukemia, except if radiotherapy occurred > 3 months previously
- Major surgery within 2 weeks before the first dose of ABL001
- The following clinical laboratory results within 3 days before the first dose of ABL001: a) For CML patients: i) Absolute neutrophil count (ANC) <= 0.5 x 109/L; ii) Hemoglobin <= 9.0 g/dL; iii) Platelets <= 75 x 109/L; b) For Ph+ ALL patients: Peripheral blood blasts > 50,000 blasts/mm3; c) Total bilirubin > 1.5 times the upper limit of the normal range (ULN), except for patients with Gilbert's syndrome, who are excluded if total bilirubin is > 3 times the ULN or if direct bilirubin is > 1.5 times the ULN; d) Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 times theULN; e) Alkaline phosphatase > 2.5 times the ULN unless considered to be not of hepatic origin; f) Creatinine > 1.5 ULN; g) Amylase values above the institutional ULN; h) Lipase values above the institutional ULN
- Treatment with medications that meet one of the following criteria and that cannot be discontinued at least one week prior to the start of treatment with ABL001 and for the duration of the study: a) Strong inducers of CYP3A4/5; b) CYP3A4/5, CYP2C8 and CYP2C9 substrates with narrow therapeutic index; c) Ph+ ALL patients maintained on stable doses of G-CSF or GM-CSF at study entry may continue therapy

- Grapefruit juice is not permitted while on study
- Residual toxic effects of Grade 2 or worse from previous therapy other than grade 2 or 3 neurotoxicity, ototoxicity, and fatigue
- Active infection, including pneumonia, requiring systemic therapy or other severe infection within 2 weeks before the first dose of ABL001
- History of significant congenital or acquired bleeding disorder unrelated to cancer.
- Known human immunodeficiency virus (HIV) positive (testing is not required)
- Serious medical or psychiatric illness likely to interfere with participation in this clinical study.
- Corrected QT interval (QTc) of > 480 milliseconds (ms) on baseline electrocardiogram(ECG) (using corrected QT interval using Fridericia [QTcF] or Bazett [QTcB]).
- Uncontrolled cardiovascular condition, including ongoing cardiac arrhythmias, congestive heart failure, angina, or myocardial infarction within the past 3 months.
- History of another active malignancy within 5 years prior to study entry with theexception of previous or concomitant basal cell skin cancer and previous carcinoma in situ treated curatively.
- History of acute pancreatitis within 1 year of study entry, chronic pancreatitis, or any ongoing pancreatic disease not considered related to the malignancies under study
- Acute or chronic liver disease (including chronic hepatitis B and C infections)
- 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 contraceptionduring dosing and for 3 days after study treatment. Highly effective contraception methodsinclude: a) Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception; b) 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; c) Male sterilization (at least 6 months prior to screening). For female subjects on the study the vasectomized male partner should be the sole partner for that subject; d) Combination of any two of the following (1+2 or 1+3, or 2+3): i) 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; ii) Placement of an intrauterine device (IUD) or intrauterine system (IUS); iii) 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 stable dosing on the same pill for a minimum of 3 months before taking study treatment.
- Sexually active males must use a condom during intercourse while taking the drug and for 3 days after stopping treatment and should not father a child in this period. A condom is required to be used also by vasectomized men in order to prevent delivery

Alter	18 Jahre und älter
Molekularer Marker	BCR-ABL1

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Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02081378 EudraCT 2013-004491-36
Therapie	ABL 001
Links	Studiendokumente zum Download (roXtra)