Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

CABL001E2201

Öffentlicher Titel	Phase II Studie zu Wirksamkeit und Sicherheit von Asciminib mit Imatinib bei Patienten mit CML-CP, bei denen mit Imatinib allein keine tiefe molekulare Remission erreicht wurde.
Wissenschaftl. Titel	A phase 2, multi-center, open-label, randomized study of oral asciminib added to imatinib versus continued imatinib versus switch to nilotinib in patients with CML-CP who have been previously treated with imatinib and have not achieved deep molecular response
Kurztitel	CABL001E2201
Studiennummer KN/ELN	LN_NN_2019_658
Studiengruppe	NN
Studienart	randomisiert, mehrarmig, offen
Studienphase	Phase II
Erkrankung	Chronische myeloische Leukämie (CML) - Chronische Phase
Leukämiestadium	.
Molekularer Marker	BCR-ABL

Einschlusskriterien

- 1. Signed informed consent must be obtained prior to participation in the study.
- 2. Male or female patients 18 years of age with a confirmed diagnosis of CML-CP defined as: • < 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 109/L (100 000/mm3) platelets • No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly
- 3. Minimum of one year (12 calendar months) treatment with imatinib first line for CML-CP (patients have to be on imatinib 400 mg QD at randomization and had no dose change in the past three months).
- 4. BCR-ABL1 levels > 0.01% IS and 1% IS at the time of randomisation as confirmed with a central assessment at screening; patients must not have achieved deep molecular response (MR4 IS) confirmed by 2 consecutive tests at any time during prior imatinib treatment. An isolated, single test result with BCR-ABL1 levels < 0.01 % (MR4 IS) is allowed, however it should not have been observed within the 9 months prior to randomization .
- 5. Patient must meet the following laboratory values before randomization: • Absolute Neutrophil Count 1.5 x 109/L • Platelets 75 x 109/L • Hemoglobin (Hgb) 9 g/dL • Serum creatinine < 1.5 mg/dL • Total bilirubin 1.5 x ULN except for patients with Gilbert's syndrome who may only be included with total bilirubin 3.0 x ULN • Aspartate transaminase (AST) 3.0 x ULN • Alanine transaminase (ALT) 3.0 x ULN • Alkaline phosphatase 2.5 x ULN • Serum lipase 1.5 x ULN. For serum lipase > ULN - 1.5 x ULN, value must be considered not clinically significant and not associated with risk factors for acute pancreatitis
- 6. Patients must have the following laboratory values (LLN) or corrected to within normal limits with supplements prior to randomization: - Potassium (potassium increase of up to 6.0 mmol/L is acceptable if associated with creatinine clearance* within normal limits) - Total calcium (corrected for serum albumin); (calcium increase of up to 12.5 mg/dl or 3.1 mmol/L is acceptable if associated with creatinine clearance* within normal limits) - Magnesium (magnesium increase of up to 3.0 mg/dL or 1.23 mmol/L if associated with creatinine clearance* within normal limits) *Creatinine clearance as calculated using Cockcroft-Gault formula

Ausschlusskriterien

- 1. Treatment failure according to European Leukemia Network criteria (Baccarani et al 2013) during imatinib treatment. • after 3 months of treatment no Complete Hematologic Response (CHR) and/or Ph+ > 95% • after 6 months of treatment BCR-ABL1 > 10% and/or Ph+ > 35% • after 12 months of treatment BCR-ABL1 > 1% and/or Ph+ > 0 • at any time loss of CHR, loss of CCyR, confirmed loss of MMR*, mutations, clonal chromosomal abnormalities in Ph+ cells (CCA/Ph+) *In 2 consecutive tests, of which one with a BCR-ABL level 1%.

- 2. Known second chronic phase of CML after previous progression to AP/BC.
- 3. Previous treatment with any TKIs other than imatinib.
- 4. History or current diagnosis of ECG abnormalities indicating significant risk or safety for subjects participating in the study such as: • History of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG) within 6 months prior to randomization • Concomitant clinically significant arrhythmias, e.g. sustained ventricular tachycardia, and clinically significant second or third degree AV block without a pacemaker • Resting QTcF 450 msec (male) or 460 msec (female) prior to randomization • Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following: • Risk factors for Torsades de Pointes including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia • Concomitant medications with a "known" risk of Torsades de Pointes per crediblemeds.org that cannot be discontinued or replaced by safe alternative medication • inability to determine the QTcF interval
- 5. 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, active or uncontrolled infection, uncontrolled clinically significant hyperlipidemia and high serum amylase).
- 6. History of acute pancreatitis within 1 year prior to randomization or past medical history of chronic pancreatitis.
- 7. History of chronic liver disease or ongoing acute liver disease.
- 8. History of other active malignancy within 3 years prior to randomization with the exception of basal cell skin cancer, indolent prostate cancer and carcinoma in situ treated curatively.
- 9. Known history of Human Immunodeficiency Virus (HIV), chronic Hepatitis B (HBV), or chronic Hepatitis C (HCV) infection. Testing for Hepatitis B surface antigen (HBsAg) and Hepatitis B core antibody (anti- HBc) will be performed at study entry. If HBsAg or anti-HBc is positive, Hepatitis B surface antibody (anti-HBs) and/or HBVDNA measurement is recommended to confirm negative viral status.
- 10. 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).
- 11. Treatment with strong inducers or inhibitors of CYP3A that cannot be discontinued or switched to a different medication at least one week prior to the start of treatment and for the duration of the study.
- 12. Patients must avoid consumption of grapefruit, Seville oranges or products containing the juice of each during the entire study and preferably 7 days before the first dose of study medications, due to potential CYP3A4 interaction with the study medications. Orange juice is allowed.
- 13. History of hypersensitivity to any of the study treatments or its excipients or to drugs of similar chemical classes.
- 14. Participation in a prior investigational study within 30 days prior to randomization or within 5 half-lives of the investigational product, whichever is longer.
- 15. Pregnant or nursing (lactating) women. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception while taking study treatment and for 14 days after stopping study medication. Highly effective contraception methods include: - see more details in section 5.2 of the protocol.
- 16. Patients who have achieved deep molecular response (MR4 IS), confirmed by 2 consecutive tests at any time during prior imatinib treatment.

Alter	>= 18 Jahre
Status	Aktiv
Beginn der Rekrutierung	01.10.2019
Sponsoren	Novartis Pharma AG
Registrierung in anderen Studienregistern	European Clinical Trials Database - EUDRACT2018-001594-24 (primäres Register)