Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

ENESTFreedom

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	ENESTFreedom
Studiennummer KN/ELN	LN_NN_2013_517
Studiengruppe	NN
Studienart	multizentrisch, einarmig, offen
Studienphase	Phase II
Erkrankung	Chronische myeloische Leukämie (CML) - Chronische Phase
Leukämiestadium	.

Ziele

- To determine the percentage of patients who are in MMR (BCR-ABL 0.1% IS (MR3)) at 48 weeks after starting the Treatment-Free Remission (TFR) phase (patients who required re-initiation of treatment will be considered as non-responders)
- To determine the percentage of patients who are in MR4.5 (BCR-ABL 0.0032% IS) at 48 weeks after starting the TFR phase (patients who required re-initiation of treatment will be considered as non-responders)
- To determine the percentage of patients who are in MMR at 96, 144 and 192 weeks after starting the TFR phase (patients who required re-initiation of treatment will be considered as non-responders)
- To determine the percentage of patients who are in MR4.5 at 96, 144 and 192 weeks after starting the TFR phase (patients who required re-initiation of treatment will be considered as non-responders)
- To determine the percentage of patients in MMR at 48, 96, 144 and 192 weeks after starting the TFR phase of nilotinib irrespective of whether or not patients required re-initiation of treatment
- To determine the percentage of patients in MR4.5 at 48, 96, 144 and 192 weeks after starting the TFR phase of nilotinib irrespective of whether or not patients required re-initiation of treatment
- To determine the percentage of patients who achieve MMR within 12 weeks of retreatment with nilotinib
- To characterize the kinetics of BCR-ABL transcripts after re-start of nilotinib therapy
- To estimate the duration of re-initiated treatment required to regain MMR after loss of MMR
- To estimate the duration of re-initiated treatment required to regain MR4.5 after loss of MMR
- To estimate the treatment-free survival (TFS) after the start of the TFR phase
- To estimate progression-free survival (PFS) after the start of the TFR phase
- To estimate overall survival (OS) after the start of the TFR phase
- To assess the safety profile during the nilotinib treatment consolidation phase, during the TFR phase and during re-initiation treatment with nilotinib
- To assess the occurrence of BCR-ABL mutations highly resistant to nilotinib (T315I, E255K/V, Y253H, F359V/C/I) or any other BCR-ABL mutations in patients who lost MMR

Einschlusskriterien

- 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

- 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 v.4.03; Serum lipase 2 x ULN i.e. equivalent to Grade 2 NCI-CTCAE v.4.03; 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) >0 1.5 x 10E9/L; Hemoglobin >= 9.0 g/dL; Platelets >= 100 x 10E9/L

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)
- 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
- 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

Alter >= 18 Jahre

Status Geschlossen

Beginn der Rekrutierung 01.03.2013

Rekrutierende Länder Deutschland
Kolumbien
Frankreich
Japan
Großbritannien
Belgien
Spanien
Italien
Griechenland
Niederlande
Polen
Österreich
Irland
Ungarn
Dänemark
Schweden
U.S.A

Fallzahl 175

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Registrierung in anderen Studienregistern	ClinicalTrials.govNCT01784068 European Clinical Trials Database - EUDRACT2012-004092-40