Kompetenznetz "Akute und chronische Leukämien"

SHORTPROTOCOL

CML V (TIGER)

Public Title	Tasigna and Interferon alpha evaluation initiated by the German CML Study Group
Scientific Title	Treatment optimization of newly diagnosed Ph/BCR-ABL positive patients with chronic myeloid leukemia (CML) in chronic phase with nilotinib vs. nilotinib plus interferon alpha induction and nilotinib or interferon alpha maintenance therapy
Short Title	CML V (TIGER)
Id KN/ELN	LN_CMLSTU_2012_498
Trialgoup	CML-Studiengruppe
Type of Trial	multicentric, randomized, open-label, double-group
Phase	Phase III
Disease	Chronic myeloid leukemia(CML) Chronic Phase
Stage of Disease	de novo/non-treated
Molecular Marker	BCR-ABL
Aim	- To evaluate the major molecular response (MMR) rate at 18 months of nilotinib compared to nilotinib+pegylated Interferon alpha (IFN) in adult patients with newly diagnosed Ph/BCR-ABL CML in chronic phase - To evaluate the feasibility to discontinue drug therapy in stable deep molecular response (MR4) after nilotinib vs. IFN maintenance therapy
Inclusion Criteria	- Male or female patients with diagnosis of CP-CML with cytogenetic confirmation of Ph chromosome [t(9;22)(q34;q11)]: 1. <15% blasts in peripheral blood and bone marrow; 2. <30% blasts plus promyelocytes in peripheral blood and bone marrow; 3. <20% basophils in the peripheral blood; >=100/nL platelets - ECOG performance status of <2 - No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly - Ph negative cases or patients with variant translocations who are BCR-ABL positive in multiplex PCR (Cross, et al 1994) are eligible as well - Pretreatment with hydroxyurea for 6 months and imatinib or nilotinib for a duration of up to 6 weeks is permitted - Age >= 18 years old (no upper age limit given) - Normal serum levels LLN (lower limit of normal) of potassium, magnesium, total calcium corrected for serum albumin, or corrected to within normal limits with supplements - ASAT and ALAT <= 2.5 x ULN (upper limit of normal) or <= 5.0 x ULN if considered due to leukemia - Alkaline phosphatase <= 2.5 x ULN unless considered due to leukemia - Total bilirubin <= 1.5 x ULN, except known Mb. Gilbert - Serum lipase and amylase <= 1.5 x ULN - Serum creatinine <= 2 x ULN - Written informed consent prior to any study procedures being performed
Exclusion Criteria	- Known impaired cardiac function, including any of the following: 1. Left ventricular ejection fraction (LVEF) < 45%; 2. Congenital long QT syndrome; 3. History of or presence of clinically significant ventricular or atrial tachyarrhythmias - Clinically significant resting bradycardia (< 50 beats per minute) - QTc>450 msec on screening ECG. If QTc > 450 ms and electrolytes are not within normal ranges before nilotinib dosing, electrolytes should be corrected and then the patient rescreened for QTc criterion - Myocardial infarction within 12 months prior to starting therapy

- Other clinical significant heart disease (e.g. unstable angina, congestive heart failure, uncontrolled hypertension)
- History of acute (i.e., within 1 year of starting study medication) or chronic pancreatitis
- Acute or chronic viral hepatitis with moderate or severe hepatic impairment (Child-Pugh scores > 6), even if controlled
- Other concurrent uncontrolled medical conditions (e.g., uncontrolled diabetes, active or uncontrolled infections, acute or chronic liver and renal disease) that could cause unacceptable safety risks or compromise compliance with the protocol
- Impaired gastrointestinal function or disease that may alter the absorption of study drug (e.g., ulcerative disease, uncontrolled nausea, vomiting and diarrhea, malabsorption syndrome, small bowel resection or gastric by-pass surgery)
- Concomitant medications with potential QT prolongation (see link for complete list: http://www.torsades.org/medicalpros/ drug- lists/printable-drug-list.cfm)
- Concomitant medications known to be strong inducers or inhibitors of the CYP450 isoenzyme CYP3A4: see link for complete list (http://medicine.iupui.edu/flockhart/table.htm)
- Patients who have undergone major surgery 2 weeks prior to starting study drug or who have not recovered from side effects of such therapy
- Patients who are pregnant or breast feeding, or women of reproductive potential not employing an effective method of birth control. (Women of childbearing potential must have a negative serum pregnancy test within 14 days prior to administration of nilotinib). Post menopausal women must be amenorrheic for at least 12 months in order to be considered of non-childbearing potential. Female patients must agree to employ an effective barrier method of birth control throughout the study and for up to 3 months following discontinuation of study drug
- Known diagnosis of human immunodeficiency virus (HIV) infection (HIV testing is not mandatory)
- Active autoimmune disorder, including autoimmune hepatitis
- Known serious hypersensitivity reactions to peginterferon alfa-2b or interferon alfa-2b or drug excipients
- Known serious hypersensitivity reactions to nilotinib
- Patients with a history of another primary malignancy that is currently clinically significant or currently requires active intervention
- Patients unwilling or unable to comply with the protocol

Age >= 18 years

Status No longer recruiting

start of Recruitment 01.08.2012

Leader

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