A Phase II, single arm, open label study of treatment-free remission in chronic myeloid leukemia (CML) chronic phase (CP) patients after achieving sustained MR4.5 on Nilotinib

Published: 03-05-2013
Last updated: 23-04-2024

The main purpose of this study is to determine the rate of treatment-free molecular remission (MMR=MR3.0) after 48 weeks following start of the TFR phase. The study further seeks to provide evidence that suspending nilotinib therapy in these...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON38513

Source
ToetsingOnline

Brief title
nilotinib suspension study after combined nilotinib/imatinib treatment

Condition

- Leukaemias

Synonym
cancer of the blood, CML

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis pharma B.V.

Intervention

Keyword: CML, MMR, MRD, nilotinib

Outcome measures

Primary outcome

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)

Secondary outcome

To evaluate the proportion of patients in TFR within 24, 36, and 48 monhs after

nilotinib cessation.

To estimate progression free survival after nilotinib cessation

To estimate treatment free survival.

Study description

Background summary

Stop imatinib study (STIM) (Mahon et al 2010) investigated feasibility of imatinib
suspension in a highly selected group of patients who achieved and maintained complete molecular response (CMR) defined as undetectable BCR-ABL levels with high sample sensitivity (10-5 or greater) for a minimum of 2 years. With a median
follow up of 34 months (Mahon et al 2011), 39% of patients have successfully remained in treatment-free remission. This provided the first evidence that achieving and maintaining deep molecular responses can lead to successful

therapy suspension. In terms of regaining molecular response, 61 patients had a molecular recurrence and 56 regained undetectable BCR-ABL transcript level after
median of 4 months on imatinib (range 0-21 months). Five patients did not return to
undetectable transcript level: four remained treatment-free with detectable transcript (range 0.05% to 0.3%) and one patient was switched to dasatinib due to
loss of CCyR (Mahon et al 2011). No loss of hematological response or progression to advanced phase was noted after stopping imatinib.

Based on results of ENESTnd [CAMN107A2303], nilotinib enables a higher proportion of newly diagnosed patients to achieve deep levels (MR4.0 (molecular response 4.0 log reduction from standardized baseline) or MR4.5) of MR vs. imatinib and potentially to be eligible for treatment suspension.
The study intends to generate data on the safety, feasibility and success of TFR
phase in a rigorously controlled manner.

Study objective

The main purpose of this study is to determine the rate of treatment-free molecular remission (MMR=MR3.0) after 48 weeks following start of the TFR phase.
The study further seeks to provide evidence that suspending nilotinib therapy in these eligible patients does not cause short- or long-term harm to them.

Study design

This is a single-arm, open label study. This study has 2 main phases: nilotinib consolidation phase (48 weeks), and nilotinib treatment-free remission (TFR) phase (week 48 * week 240).

Intervention

Stop nilotinib treatment

Study burden and risks

The biggest risk in this study is recurrence of CML, but from previous studies, it is known that with reinitiation of therapy, complete remission can be induced quickly again.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Male or female patients *18 years of age
ECOG performance status of 0-2
Patient with diagnosis of BCR-ABL positive CML
Patient has received minimum of 3 years of tyrosine kinase inhibitor treatment (first with imantinib and then switched to nilotinib) since initial diagnosis
Minimum of 2 calendar years of nilotinib treatment before study entry
Patient has achieved MR4.5 (local laboratory assessment) during nilotinib treatment, and determined by a Novartis designated central PCR lab assessment at screening.
Adequate end organ function as defined by:
* Direct bilirubin * 1.5 x ULN
* SGOT(AST) and SGPT(ALT) * 3 x ULN
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 above LLN limits or corrected to be within normal limits with supplements prior to
first dose of study medication:
* Potassium
* Magnesium
* Total calcium (corrected for serum albumin)
Patients must have normal marrow function as defined:
* Absolute Neutrophil Count (ANC) * 1.5 x 109/L
* Hemoglobin * 9.0 g/dL
* Platelets * 100 x 109/L

Exclusion criteria

Prior AP, BC or allo-transplant
Patient has documented MR4.5 at the time when switched from imatinib to nilotinib
Patients with known atypical transcript
Mutation(s) (T351I, E255K/V, Y253H, F359C/V) detected if a testing was done in the past (there is no requirement to perform
mutation testing at study entry if it was not done in the past)
Dose reductions due to neutropenia or thrombocytopenia in the past 6 months
Patient ever attempted to permanently discontinue imatinib or nilotinib treatment
Known impaired cardiac function
History of acute pancreatitis
Known presence of a significant congenital or acquired bleeding disorder unrelated to cancer
History of other active malignancy within 5 years prior to study entry
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 study entry.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	3
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	tasigna
Generic name:	nilotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-05-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-003186-18-NL
ClinicalTrials.gov	NCT01698905
CCMO	NL44493.029.13