A multi-center, open label, non-controlled phase II study to evaluate efficacy and safety of oral nilotinib in pediatric patients with newly diagnosed Ph+ chronic myelogenous leukemia (CML) in chronic phase (CP) or with Ph+ CML in CP or accelerated phase (AP) resistant or intolerant to either imatinib or dasatinib

Published: 16-12-2013
Last updated: 22-04-2024

Primary objectives:* To assess efficacy of nilotinib in pediatric patients with Ph+ CML CPresistant or intolerant to either imatinib or dasatinib.* To assess efficacy of nilotinib in pediatric patients with Ph+ CML APresistant or intolerant to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON47717

Source
ToetsingOnline

Brief title
CAMN107A2203

Condition

- Leukaemias

Synonym
Bloodcancer, proliferation of blood cells

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Children, CML, Nilotinib, Phase II

Outcome measures

Primary outcome

* Rate of MCyR by 6 months

* Rate of complete hematological response (CHR) by 3 months

* Rate of MMR by 12 months by PCR analysis. MMR is defined as * 0.1%

BCR-ABL/control gene % by international scale, measured by RQ-PCR which is

equivalent to * 3 log reduction of BCR-ABL transcript from standardized

* Rate of MCyR by 6 months

Secondary outcome

* Time to response, duration of response, time to disease progression, overall

survival

* Rate of MCyR and CCyR in newly diagnosed Ph+ CML CP and in Ph+ CML CP AP

patients resistant/intolerant to either imatinib or dasatinib by 6, 12* and 24

months

* Rate of MMR by 3, 6, 9, 12* and 24 months in newly diagnosed Ph+ CML CP and Ph+ CML CP and AP patients resistant/intolerant to either imatinib or dasatinib

* Rate of CHR by 3*, 6, 9, 12 and 24 in newly diagnosed Ph+ CML CP and in Ph+ CML CP and AP patients resistant/intolerant to either imatinib or dasatinib

* Population PK parameters of nilotinib

* Pharmacodynamics (BCR-ABL transcript levels determined with standard protocols in peripheral blood and bone marrow)

* Safety and tolerability: incidence and severity of adverse events, as assessed by patient symptoms, physical exam assessments, abnormal laboratory tests, echocardiograms and electrocardiograms

* Mutational assessments of BCR-ABL

* Questionnaire on acceptability (including palatability) of dose forms used after first dose, cycle 1 and cycle 12

Study description

Background summary

The purpose of the phase II study is to characterize efficacy, safety and PK parameters of nilotinib in the Ph+ CML pediatric patient population (from 1 to <18 years). The rationale for the development of nilotinib in pediatric Ph+ CML is that nilotinib has shown a positive benefit/risk profile in both adult patients with Ph+ CML in CP or AP resistant or intolerant to prior therapy including imatinib and adult patients with newly diagnosed Ph+ CML CP.

Study objective

Primary objectives:
* To assess efficacy of nilotinib in pediatric patients with Ph+ CML CP resistant or intolerant to either imatinib or dasatinib.
* To assess efficacy of nilotinib in pediatric patients with Ph+ CML AP

resistant or intolerant to either imatinib or dasatinib.
* To assess efficacy of nilotinib in pediatric patients with newly diagnosed Ph+ CML CP.

Secondary objectives:
* To characterize efficacy in pediatric patients with Ph+ CML.
* To further characterize PK in pediatric patients with Ph+ CML.
* To identify emerging signs of resistance to nilotinib.
* To describe acceptability of the study drug formulation.
* To further characterize safety and tolerability of nilotinib in pediatric patients with Ph+ CML-.* To assess long term effect on growth, development and maturation of nilotiib treatment in pediatric patients with Ph+CML.

Study design

This is a multi-center open label, non-controlled study of nilotinib. Nilotinib will be administered at 230 mg/m2 p.o., twice daily, rounded to the nearest 50 mg dose (to a maximum dose of 400mg) for up to 66 cycles (1 cycle is 28 days).

Intervention

Children will be treated with oral nilotinib long as they will benefit from it. Response assessment every 28 days.

Study burden and risks

Risk:
Side effects of the study medication (see also the dose-limiting toxicities described on page 34, Table 6-2), drawing blood samples and tissue biopsies. Het collection of blood can cause a bruise, bleeding at the site or blood clothing. These usually disappear naturally.

Burden:
-study visits at least 1 time per 28 days for 2 years after proceeding though the screening.
-blood draws for lab tests every visit.
-other assesments such as tissue biospies and ECGs

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Newly diagnosed and untreated Ph+ CML CP or Ph+ CML CP or AP resistant or intolerant to either imatinib or dasatinib;2. Karnofsky or Lansky * 50;3. Adequate renal, hepatic and pancreatic function;4. Potassium, magnesium, phosphorus and total calcium values * LLN (lower limit of normal);5. Written informed consent;Additional inclusion criteria are defined in the protocol.

Exclusion criteria

1. Treatment with strong CYP3A4 inhibitors or inducers;2. Use or planned use of any medications that have a known risk or possible risk to prolong the QT interval;3. Acute or chronic liver, pancreatic or severe renal disease;4. History of pancreatitis or chronic pancreatitis.;5. Impaired cardiac function;6. No evidence of active graft vs host in less than 3 months since the last Stem Cell Transplant;7. Total body irradiation (TBI) or craniospinal radiation therapy in < 6months. Hypersensitivity to the active ingredient or any of the excipients including lactose;Additional exclusion criteria are defined in the protocol.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2014
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nilotinib
Generic name:	AMN107
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	16-12-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	20-12-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-03-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-05-2016
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-05-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	29-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2013-000200-41-NL
CCMO	NL45150.078.13