A Phase II Study of Dasatinib Therapy in Children and Adolescents with Newly Diagnosed Chronic Phase Chronic Myelogenous Leukemia or with Ph+ Leukaemias Resistant or Intolerant to Imatinib

Published: 02-07-2009
Last updated: 06-05-2024

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

Summary

ID

NL-OMON47600

Source
ToetsingOnline

Brief title
CA180-226

Condition

- Leukaemias

Synonym
Leukemias

Research involving

Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharma Industry

Intervention

Keyword: Children, Dasatinib, Leukemia, Ph+

Outcome measures

Primary outcome

The primary objective of this study is to estimate the rate of response to dasatinib in children and adolescents with certain types of leukaemia, whose disease is either resistant to, intolerant to, or relapsed after previous imatinib therapy or are newly diagnosed and treatment naïve.

Secondary outcome

The secondary objectives of this study are: to assess safety and tolerability in the above patient groups; to evaluate additional measures of response/effectiveness: best cytogenetic and haematological response rates; time to response; duration of response; progression-free survival; overall survival; rates of complete and major molecular response (response at the DNA level); to look at Bcr-abl mutations at baseline, at progression or end of treatment and to explore the role of mutations as predictors of response.

Study description

Background summary

Dasatanib targets leukaemias that carry a genetic defect commonly known as the

'Philadelphia chromosome'. These types of leukaemias can be difficult to cure and are known to become resistant to the currently available treatment drug, called imatinib. Adult studies and preliminary results from studies in children have shown dasatanib can be effective in treating this type of leukaemia. This study will aim to find out if dasatanib is effective for this group of patients in a larger, more statistically valid, number of patients. It will also look at whether dasatinib is effective in newly diagnosed, treatment naïve children and adolescents with chronic phase CML for whom immediate hematopoetic stem cell transplant (HSCT) is not available. An additional 30 newly diagnosed patients will be included to test the new dasatinib powder for oral suspension (PFOS).

Study objective

The main objective of this study is to estimate the rate of response to dasatinib in children and adolescents with certain types of Ph+ leukaemia either whose disease is resistant to, intolerant to or relapsed after previous imatinib therapy or are newly diagnosed and treatment naïve.

Study design

Open*label, non-randomised Phase II multi*centre study in children and adolescents with Ph+ leukaemia with either resistance or intolerance to the standard treatment Imatinib or newly diagnosed and treatment naïve. Patients will either receive dasatinib orally on a daily basis or in solution form (PFOS) for as long as they are receiving benefit. Approximately 139 patients will be enrolled in total, 30 newly diagnosed patients will receive PFOS.

Intervention

Cohort 1: Dasatinib 60mg/m2 orally once daily
Cohort 2: Dasatinib 80mg/m2 orally once daily
Cohort 3a: Dasatinib 60mg/m2 orally once daily
Cohort 3b: Dasatinib 72mg/m2 in solution form once daily
Patients in Cohorts 1,2 and 3a remaining on study can choose to be switched to the solution form at a dose of 72mg/m2 if on the 60mg/m2 oral dose or 96mg/m2 if on the 80mg/m2 oral dose.

Study burden and risks

Dasatinib has been shown to be well tolerated in adults and children, with a high efficacy in adult Ph+ disease. It has also shown efficacy in a few paediatric studies with preliminary analysis showing better tolerability in children. In light of the high efficacy in adults and favourable safety profile seen so far in children, together with the urgent need to identify new effective treatments for these high risk subjects, the risk:benefit ratio is

considered to be very favourable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Diagnosis:
Cohort 1: Subjects must have Ph+ CP-CML
Cohort 2: Subjects must have Ph+ ALL or Ph+ AP- or BP-CML
Cohort 3a: newly diagnosed treatment-naive chronic phase chronic myelogenous leukemia (CP-CML)
Cohort 3b: sub-cohort of 30 newly diagnosed treatment-naive chronic phase

chronic myelogenous leukemia (CP-CML), who will receive dasatinib powder for oral suspension (PFOS), Subjects in Cohorts 1 and 2 must have proven resistance or intolerance to imatinib
(2) Lansky or Karnofsky scale > 50
(3) Life expectancy * 12 weeks
(4) Subjects must have recovered to baseline or Grade 1 (NCI CTCAE, version 3.0) from the toxicities (except alopecia) resulting from recent therapies, including chemotherapy, hormonal therapy, immunotherapy, biological therapy or investigational product and radiation therapy
(5) Serum Na, K, Na, HC03, Mg, P and Ca levels within institutional normal limits and AST, ALT, bilirubin, serum creatinine * Grade 2 (NCI CTCAE, Version 3.0)

Exclusion criteria

(1) Subjects for whom potentially-curative therapy is available, including hematopoietic stem-cell transplantation (HSCT)
(2) Symptomatic central nervous system (CNS) involvement (except if signs and symptoms are from isolated leptomeningeal disease)
(3) Isolated extramedullary disease, with < 5% blasts in bone marrow
(4) Any serious uncontrolled medical disorder that would impair the ability of the subject to receive protocol therapy
(5) Prior therapy with dasatinib
(6) Any investigational agent or any other anti-cancer agent within 14 days prior to treatment start. Imatinib mesylate may be continued up to 7 days before treatment start, or, in the presence of rising peripheral blast cells, imatinib may be continued up to 2 days before treatment start. If required for control of peripheral blast cells, hydroxyurea, corticosteroids, 6-mercaptopurine or 6-thioguanine may be given up to 2 days before treatment start.
(7) Subjects requiring ongoing medications which may:
-Have a known risk of causing QTc prolongation
-Irreversibly inhibit platelet function, or anticoagulants (Does not apply to low-dose heparin for prophylaxis or to heparin flushes for i.v. lines)
(8) Sexually active females of child-bearing potential that are unwilling or unable to use an acceptable method to avoid pregnancy.
(9) Sexually active fertile malesnot using effective birth control, if their partners are of child-bearing potential.
(10) Cohort 3a and b: no prior chemotherapy, immunotherapy, or radiotherapy for CML with the exception of hydroxyurea

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):	25-11-2011
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sprycel
Generic name:	dasatinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-07-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-09-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-02-2010
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-05-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-11-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-12-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-02-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	13-08-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-11-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-02-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-02-2014
Application type:	Amendment
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:	12-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-05-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-06-2015

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-07-2017
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:	25-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-02-2019
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	07-05-2021
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	EUCTR2008-002260-33-NL
ClinicalTrials.gov	NCT00777036
CCMO	NL28377.078.09