Development and introduction of a pediatric liquid formulation of mercaptopurine for treatment of leukemia

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The aim of this study is to improve 6MP treatment in pediatric leukemia patients, by developing and licensing a pediatric liquid formulation of 6MP, assessing its stability and bioequivalence, and ensuring a nationwide introduction of the new...

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

Summary

ID

NL-OMON35236

Source
ToetsingOnline

Brief title
6mp formulation

Condition

- Leukaemias

Synonym
acute lymphoblastic leukemia; leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: stichting kika

Intervention

Keyword: formulation, leukemia, mercaptopurin, pediatrics

Outcome measures

Primary outcome

Bioequivalence will be assessed by determining blood levels of the active metabolites of 6MP in red blood cells. Two-weekly leukocyte counts will be performed to monitor hematological toxicity. Compliance and acceptance of the different formulations by children and parents will be assessed by questionnaires.

Secondary outcome

Acceptation by the patient

Study description

Background summary

Patients with acute lymphoblastic leukemia (ALL) are currently treated in the Netherlands according to the Dutch Childhood Oncology Group (DCOG) ALL10 protocol, in which the oral cytotoxic drug 6-mercaptopurine (6MP) is administered daily, for a period between one and two years. Because of the lack of a commercially available pediatric formulation of 6MP, 6MP needs to be prepared as capsules containing the specific dosage needed for each patient by community pharmacies. Every 2 weeks the dosage of 6MP is adapted according to the leukocytes count. Since most pharmacies are not equipped to prepare capsules of cytotoxic compounds such as 6MP, the availability (within an acceptable time-window) of 6MP in the correct dosage, after discharge of the patient and after every dosage adaptation, is problematic and may lead to inadequate patient care. Moreover, in order to prepare a drinking solution for younger children, the parents have to dissolve the capsules at home with water before administration. This may lead to unwanted drug exposure of the parents, and may also increase the risk for errors in dosing or administration.

Study objective

The aim of this study is to improve 6MP treatment in pediatric leukemia patients, by developing and licensing a pediatric liquid formulation of 6MP, assessing its stability and bioequivalence, and ensuring a nationwide introduction of the new formulation.

Study design

A crossover open label study will be performed.

Intervention

Patients will receive 4 weeks treatment with capsules, followed by 4 weeks treatment with liquid formulation, or vice versa.

Study burden and risks

The burden and risks for the patients are minimal. Every patient will receive 6MP as part of standard clinical care. Blood sampling will be done using the existing vascular access ports, during regular hospital visits. A diary has to be filled in during the study period to record side effects and compliance issues.
The study needs to be performed in this patient population, because of the established indication for 6MP in pediatric leukemia and the problems associated with drug formulations in children.

Contacts

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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

- histologically or cytologically confirmed acute lymphatic leukemia
- inclusion in dcog all10 protocol or interfant 06
- available venous access port
- ALAT and ASAT <1000 IU/l
- written informed consent

Exclusion criteria

- patient or parent refusal
- pre-existing liver disease

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2009
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Puri-nethol
Generic name:	6 mercaptopurine

Ethics review

Approved WMO Date:	29-08-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-11-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-10-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-10-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-03-2010

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2010
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	EUCTR2008-000424-86-NL
CCMO	NL21347.078.08