Clofarabine added to prephase and consolidation therapy in acute lymphoblastic leukemia in adults.

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

Summary

ID

NL-OMON41476

Source
ToetsingOnline

Brief title
HOVON 100 ALL / EORTC 06083

Condition

- Leukaemias
- Leukaemias

Synonym
Acute lymphoblastic leukemia

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: HOVON,Sanofi/Genzyme

Intervention

Keyword: Acute lymphoblastic leukemia, adults, clofarabine

Outcome measures

Primary outcome

1. Feasiblilty of clofarabine when added to standard phrephase chemotherapy.

2. Event-free survival (EFS) (i.e., time from registration to induction

failure, death or relapse whichever occurs first).

Secondary outcome

- Response

- Overall survival (OS) mesured form the time of registration

- Disease-free interval (duration of the first CR) measured form the time of

achievement of CR to day of relapse or death from any cause (whichever occurs

first).

- Outcome of treatment in relation to minimal residual disease measurements.

- Evaluation of toxicities and treatment related mortality.

Study description

Background summary

In this phase III study the drug clofarabine is added to the standard chemotherapy for remission induction therapy of adults age below 70 years, with acute lymphoblastic leukemia. The aim of this study is to examine whether the treatment outcome improves by adding clofarabine. Clofarabine is an effective drug that, if given as singel medication to the patients with relapsed disease induces remissions. In this study clofarabine is given in combination with the standard prephase chemotherapy and subsequently as monotherapy in a distinct consolidation cycle. In the first part of the study the feasebility of

clofarabine will be examined compared to the treatment without clofarabine in a randomized design. In the second part of the study the phase III will be done with the feasible dose level. Minimal residual disease measurements at previously defined timepoints will be performed to be able to correlate the effect of therapy.

Study objective

Primary objectives:
1.The fesibility of clofarabine when given together with standard prephase chemotehrapy in a prospective comparison to standard prephase chemotherapy (prednison).
2.To evaluate the effect of clofarabin when combined with prephase chemotherapy and as a single consolidation courase as regards clinical outcome ("event-free survival") in comparison to prephase / consolidation without clofarabine in a phase III study.

Secondary objectives:
- To improve the molecular response rate of adult ALL following RI by the addition of i.v. clofarabine to standard prephaseprephase and consolidation therapy
- To improve DFS, and OS in adult ALL patients by the addition of i.v. clofarabine to the
standard prephase and consolidation therapy
- To document safety and toxicity of adding clofarabine to standard prephase and consolidation therapy in adult ALL
- To assess and compare clinical outcome of patients with and without an HLA-identical sibling in a donor vs no-donor analysis

Study design

1. Comparative, randomized feasibility study of remission induction chemotherapy combined with clofarabine.
2. Multicenter, phase III study at the feasible dose level of clofarabin in a prospective randomised approach.

Intervention

In the experimantal arm intraveniously administered clofarabine will be added to standard prephase chemotherapy.

The study starts at a dose level of 20 mg/m2, and if possible escalating to 30 mg/m2. If 20 mg/m2 is not feasible we will study 15 mg/m2. At each dose level the decision to stop or escalate will be made bye the DSMB based on a comparison of DLTs in either arm.

Study burden and risks

The addition of lofarabine can increase the possibility of toxicities. Possibly not all toxicities are known, although clofarabine is given before and seems to be tolerated well. Clofaraine causes nausea and alopecia. Further it reduces the production of blood as other chemotherapy does.

Further toxicities of clofarabine known from previous research are lier dysfunction.
At time of the normal bone marrow punctions at start a limited amount of extra bone marrow will be collected via the same needle. this is abouth 10 ml.
For monitoring of Asparaginase activity blood will be taken for during induction and intensificaion I and II for the young patients en for the older patients 4 times during consolidatie II. This will be combined with the regular blood takes, if possible.

Contacts

Public
HOVON

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
HOVON

De Boelelaan 1117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

- Patients aged 18 to 70 years inclusive
- Primary previously untreated B or T-lineage ALL (excluding ALL with mature B-cell phenotype, but including Philadelphia positive or BCR-ABL positive ALL) or previously untreated T-LBL (pretreatment with prednisone for 7 days is allowed)
- WHO performance status 0 - 2
- Adequate renal and hepatic function tests as indicated by the following laboratory values:
- Serum creatinine <=1.0 mg/dl (<= 88.7 micromol/L); if serum creatinine >1.0 mg/dl (>88.7 micromol/L), then the glomerular filtration rate (GFR) must be >60 ml/min/1.73 m2 as calculated by the Modification of Diet in Renal Disease equation where the predicted GFR (ml/min/1.73 m2) = 186 x (Serum Creatinine in mg/dl)-1.154 x (age in years)-0.023 x (0.742 if patient is female) x (1.212 if patient is black)
NOTE: if serum creatinine is measured in micromol/L, recalculate it in mg/dl according to the equation: 1 mg/dl = 88.7 micromol/L) and used above mentioned formula.
- Serum bilirubin <= 1.5 × upper limit of normal (ULN)
- Aspartate transaminase (AST)/alanine transaminase (ALT) <= 2.5 × ULN
- Alkaline phosphatase <= 2.5 × ULN
- Negative pregnancy test at inclusion, if applicable
- Written informed consent

Exclusion criteria

- Mature surface Ig positive B-cell leukemia/lymphoma
- Acute undifferentiated leukemia
- Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease)
- Severe pulmonary dysfunction (CTCAE grade III-IV)
- Severe neurological or psychiatric disease
- History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma
- Active, uncontrolled infection
-Patient known to be HIV-positive
-Patient is a lactating woman
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- Unwilling or not capable to use effective means of birth control (all men, all premenopausal women under the age of 50 need contraception for two years after the last period, and women older than 50 yrs for at least one year)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-10-2009
Enrollment:	285
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Evoltra
Generic name:	clofarabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-04-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-08-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	05-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-02-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-08-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-04-2012

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-05-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2015
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	EUCTR2008-005798-36-NL
CCMO	NL27016.078.09