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Treatment of acute lymphoblastic leukemia (ALL) in adults age 40 - 70 years inclusive with chemotherapy including a "pre-induction course" for rapid tumor load reduction and prolonged maintenance chemotherapy

Submission date
20/08/2010

Recruitment status
No longer recruiting

Registration date
06/09/2010

Overall study status
Completed

Last Edited
30/03/2017

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Acute lymphoblastic leukaemia (ALL) is a type of cancer that affects the white blood cells. The outcome of treatment in adults is much worse than in children. The long-term survival of older patients after intensive chemotherapy is less than 30%, and patients aged over 60have a dismal 2-year survival rate of only 10 - 15%. They therefore are often not exposed to the toxicity (side effects) of aggressive chemotherapy. However, this might be improved markedly by a simple trick called a pre-induction course. This consists of administering cytostatic drugs with a different mechanism of action in order to rapidly reduce the tumour load before starting the regular treatment. Another, although not unique, characteristic of the treatment is the prolonged use of (less intensive) maintenance chemotherapy. With this approach, a 5-year survival rate of over 60% was obtained in adults of any age including patients over 60. The aim of this study is to find out whether this result could be reproduced for ALL patients aged over 40 and to investigate whether the toxicity of this treatment was manageable in patients aged up to 70.

Who can participate?
Patients aged between 40 and 70 with newly diagnosed ALL

What does the study involve?
Participants start treatment with a combination of the drugs cytarabine (AraC) and etoposide (VP16) at relatively low doses on days 1 and 8, and methotrexate (MTX) at an intermediate dose on day 4 and 11. On day 15, a variant of the commonly used anti-ALL treatment with oncovin, prednisone, and adriamycine (OPA) is started. This causes a profound but temporary suppression of the bone marrow leading to severe depletion of blood cells. Soon after recovery of the bone marrow, the OPA course is repeated once, followed by a consolidation course of AraC (at a higher dose than the pre-induction) and asparaginase. Thereafter, maintenance treatment with

courses of 4 weeks duration consisting of vincristine, prednison, MTX, and 6-mercaptopurine are used for 2 years. Patients in complete remission, i.e. with no signs of ALL, are then eligible for a bone marrow transplant if they have a suitable donor.

What are the possible benefits and risks of participating?
Based on the results of earlier studies, participation in the study could probably increase their chances of survival. However, these results need to be confirmed. Toxicity in patients aged over 60 could be higher than expected, counterbalancing a possible gain in effectiveness.

Where is the study run from?
University Medical Center Groningen (Netherlands)

When is the study starting and how long is it expected to run for?
October 2005 to June 2011

Who is funding the study?
1. Dutch Haemato-Oncology Association (Netherlands)
2. Dutch Cancer Fund (Netherlands)

Who is the main contact?
Dr Simon Daenen

Study website
http://www.hovon.nl

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Ho71

Study information

Scientific Title
Treatment of acute lymphoblastic leukemia (ALL) in adults age 40 - 70 years inclusive with chemotherapy including a "pre-induction course" for rapid tumor load reduction and prolonged maintenance chemotherapy: a phase II multicentre study

Acronym
HOVON 71 ALL

Study objectives
The hypothesis to be tested is that treatment with 1 prephase course, 2 induction courses, 1 consolidation course, Allogenic Stem Cell Transplantation (allo-SCT) or maintenance treatment is feasible, and efficacy meets the expectations as described in the protocol.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Medical Ethics Committee (MEC) of University Medical Centre Groningen, 22/08/2005, ref: METc 2005/063

Study design
Prospective phase II multicentre non-randomised trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Acute Lymphoblastic Leukemia

Interventions
Patients will be treated with the following courses:
1. Pre-induction course consisting of Ara-C 200 mg/m2/day, 2 days, etoposide 120 mg/m2/day, 2 days, MTX 500 mg/m2/day, 2 days and leucovorin.
2. 2 ODA induction courses consisting of dexamethasone 8-12 mg/day, 21 days, vincristine 1 mg

/day, 3 days and adriamycine 30-40 mg/m2/day, 3 days.
3. Consolidation course consisting of Ara-C 1000 mg/m2/12 hr, 2 days and L-asparaginase 6000 IU /m2/day, 10 days.
4. Patients will then either go for allo-SCT or maintenance treatment.
4.1. Maintenance treatment consisting of 30 courses every 4 weeks, which are 23 regular (R) courses (prednisone 1 mg/kg/day, 7 days, vincristine 1-2 mg/day, 1 day, MTX 15 mg/m2/day, 3 days, 6-Mercaptopurine 75 mg/m2/day, 21 days) interspersed with 4 courses of intensification A (prednisone and vincristine same dose and schedule as regular, Ara-C 200 mg/m2/day, 3 days and etoposide 120 mg/m2/day, 3 days) and 3 courses of intensification B (prednisone and vincristine same dose and schedule as regular, mitoxantrone 8 mg/m2/day, 1 day, cyclophosphamide 750 mg/m2/day, 1 day and a medication free period of 20 days).

Intervention Type
Drug

Phase
Not Applicable

Primary outcome measure
Disease-free survival (i.e. time from achievement of complete response [CR] to day of relapse or death from any cause, whichever comes first)

Secondary outcome measures
1. CR rate after remission induction and consolidation
2. Toxicity profile related to each treatment step and intervals between treatment steps
3. Event-free survival (i.e. time from registration until no CR on protocol, relapse or death, whichever comes first); Event-free survival for patients without a CR is set at one day
4. Overall survival measured from time of registration
5. Outcome of patients with a reduced intensity conditioning allogeneic stem cell transplantation

Overall study start date
21/10/2005

Completion date
30/06/2011

Eligibility

Key inclusion criteria
1. Age 40 - 70 years inclusive
2. Primary previously untreated ALL*
3. WHO performance status 0, 1, or 2
4. Negative pregnancy test at inclusion if applicable
5. Written informed consent

*Patients with mediastinal mass defining the so-called T-lymphoblastic leukemia/lymphoma are eligible for this trial. ALL patients with Philadelphia chromosome - t(9;22) and variants - are also eligible for this trial. However, when an alternative trial for Philadelphia chromosome positive patients becomes available, patients should be included in that trial by preference.

Participant type(s)

Patient

Age group
Adult

Sex
Both

Target number of participants
55

Key exclusion criteria
1. Mature B-cell ALL, i.e. Burkitt leukemia/lymphoma
2. Acute undifferentiated leukemia (AUL)
3. Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease)
4. Severe pulmonary dysfunction (Common Terminology Criteria for Adverse Events [CTCAE] grade III-IV)
5. Severe neurological or psychiatric disease
6. Significant hepatic dysfunction (serum bilirubin or transaminases ≥ 3 times normal level) except when caused by leukemic infiltration
7. Significant renal dysfunction (serum creatinine ≥ 3 times normal level after rehydration and correction of hyperuricemia)
8. History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma
9. History of anthracycline use exceeding a cumulative dose of 300 mg/m2 doxorubicin (or its biological equivalent)
10. Active, uncontrolled infections
11. Patient known to be HIV-positive

Date of first enrolment
21/10/2005

Date of final enrolment
30/06/2011

Locations

Countries of recruitment
Belgium

Netherlands

Study participating centre
University Medical Center Groningen
Groningen
Netherlands
9700 RB

Sponsor information

Organisation
Dutch Haemato-Oncology Association (Stichting Hemato-Oncologie Volwassenen Nederland) (HOVON) (Netherlands)

Sponsor details
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Sponsor type
Research council

Website
http://www.hovon.nl

ROR
https://ror.org/056kpdx27

Funder(s)

Funder type
Research organisation

Funder Name
Dutch Haemato-Oncology Association (Stichting Hemato-Oncologie Volwassenen Nederland) (HOVON) (Netherlands)

Funder Name
Dutch Cancer Fund (KWF) (Netherlands)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2012		Yes	No