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Randomised induction and post induction therapy in older patients (greater than or equal to 61 years of age) with Acute Myelocytic Leukaemia (AML) and Refractory Anaemia with Excess of Blasts (RAEB, RAEB-t)

Submission date
20/12/2005

Recruitment status
No longer recruiting

Registration date
20/12/2005

Overall study status
Completed

Last Edited
19/10/2018

Condition category
Cancer

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

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.hovon.nl

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR212; HO43

Study information

Scientific Title
Randomised induction and post induction therapy in older patients (greater than or equal to 61 years of age) with Acute Myelocytic Leukaemia (AML) and Refractory Anaemia with Excess of Blasts (RAEB, RAEB-t)

Acronym
HOVON 43 AML/SAKK 30/01

Study objectives
1. The first hypothesis to be tested is that the outcome in arm B is better than in arm A.
2. The second hypothesis to be tested is that the outcome in arm two is better than in arm one.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Prospective randomised, active controlled, parallel group, multicentre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Acute Myeloid Leukaemia (AML)

Interventions

Patients will be randomised on entry for induction between:

Arm A:
Cycle I: conventional type daunomycin-cytarabine schedule
Cycle II: intermediate dose cytarabine

Arm B:
Cycle I: daunomycin at escalated dose with standard dose cytarabine
Cycle II: intermediate dose cytarabine

Patients attaining Complete Response (CR) and remaining in CR after cycle II will be randomised between:

Arm one: no further treatment
Arm two: three dosages of Gemtuzumab Ozogamicin (GO, Mylotarg) at four week intervals

For patients with an Human Leukocyte Antigen (HLA) identical sibling donor, an allograft with non-myeloablative conditioning, will be available depending on the active involvement in allotransplantation per centre (optional per centre).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Cytarabine, daunomycin, gemtuzumab ozogamicin

Primary outcome measure
Endpoint for the comparison of induction treatment arm B with arm A:
Event-free survival (i.e. time from registration to induction failure, death or relapse whichever occurs first); the time to failure of patients with induction failure is set at one day.

Endpoint for the comparison of post induction maintenance treatment with GO with no further treatment: disease-free survival measured from the date of second randomisation to relapse or death from any cause.

Secondary outcome measures
Endpoints for the comparison of induction treatment arm B with arm A:
1. Response and especially CR to chemotherapy cycles I and II
2. Overall survival measured form the time of registration
3. Disease-free interval (duration of the first CR) measured from the time of achievement of CR to day of relapse or death from any cause (whichever occurs first)
4. Probability of complete response, relapse, death in CR1, event-free survival, disease-free survival and overall survival will also be assessed in relation to age (61 - 70, 70 - 80, above 80), cytogenetic abnormalities, CD33-positivity of AML (phenotype), P-glycoprotein (PgP) positivity
5. Toxicities and treatment related mortality
6. Time to haematopoietic recovery (Absolute Neutrophil Count [ANC] 0.5 and 1.5 x 10^9/l; platelets 50 and 100 x 10^9/l) after each treatment cycle
7. Number of platelet transfusions and last day of platelet transfusion after each cycle

Endpoints for the comparison of post induction maintenance treatment with GO with no further treatment:
1. Overall survival measured from the date of second randomisation.
2. Probability of relapse and death in first CR from date of second randomisation calculated as competing risks
3. Number and duration of hospitalisation as well as transfusion requirements (red cell and platelet transfusion)

Overall study start date
09/10/2000

Completion date
01/11/2005

Eligibility

Key inclusion criteria
1. Age 61 years or more
2. Subjects with a cytopathologically confirmed diagnosis of AML (M0-M2 and M4-M7, FAB classification), or with Refractory Anaemia with Excess of Blasts (RAEB) or Refractory Anaemia with Excess of Blasts in transformation (RAEB-t) with an International Prognostic Scoring System (IPSS) score of greater than or equal to 1.5
3. Subjects with a secondary AML progressing from antecedent Myelodysplasia (MDS) and biphenotypic leukemia are eligible. Antecedent MDS refers to any antecedent haematological disease of at least four month duration
4. World Health Organisation (WHO) performance status less than or equal to two
5. Written informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
800

Key exclusion criteria
1. Previous induction treatment for AML/MDS
2. Prior chemotherapy within six months of study entry
3. Previous polycythemia rubra vera
4. Primary myelofibrosis
5. Blast crisis of chronic myeloid leukemia
6. AML-FAB type M3 or AML with cytogenetic abnormality t(1517) translocation
7. Impaired hepatic or renal function as defined by:
a. Alanine Aminotransferase (ALT) and/or Aspartate Aminotransferase (AST) greater than 25 x normal value

b. Bilirubin greater than 2 x normal value
8. Serum creatinine greater than 2 x normal value (after adequate hydration), unless these are most likely caused by AML organ infiltration
9. Concurrent severe and/or uncontrolled medical condition (e.g., uncontrolled diabetes, infection, hypertension, etc.,)
10. Cardiac dysfunction as defined by:
10.1. myocardial infarction within the last six months of study entry, or
10.2. reduced left ventricular function with an ejection fraction less than or equal to 50% as measured by Multiple Gated Acquisition (MUGA) scan or echocardiogram (another method for measuring cardiac function is acceptable)
11. Unstable angina
12. Unstable cardiac arrhythmias

Date of first enrolment
09/10/2000

Date of final enrolment
01/11/2005

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Centre
Rotterdam
Netherlands
3008 AE

Sponsor information

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

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Sponsor type

Research organisation

Website
http://www.hovon.nl/

ROR
https://ror.org/056kpdx27

Funder(s)

Funder type
Research organisation

Funder Name
Koningin Wilhelmina Fonds (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?
Plain English results				No	Yes
Results article	results	24/09/2009		Yes	No
Results article	results	01/04/2010		Yes	No