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A phase II multicentre study to assess the tolerability and efficacy of the addition of bevacizumab to standard induction therapy in Acute Myeloid Leukaemia and high risk myelodysplastic syndrome above 60 years

Submission date 07/03/2007	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 07/03/2007	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 19/07/2021	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

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
2006-001777-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HO81

Study information

Scientific Title
A phase II multicentre study to assess the tolerability and efficacy of the addition of bevacizumab to standard induction therapy in Acute Myeloid Leukaemia and high risk myelodysplastic syndrome above 60 years

Acronym
HOVON 81 AML

Study objectives
1. Evaluation of the safety and tolerability of bevacizumab added to standard induction chemotherapy
2. Evaluation of the effect of bevacizumab on the Complete Response (CR) rate

The hypothesis to be tested is that arm B is tolerable and that the outcome in arm B is better than in arm A.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the local medical ethics committee (Medische Ethische Toetsingscommissie VU Medisch Centrum) on the 7th December 2006 (ref: 2006/215).

Study design
Randomised, active controlled, parallel group, multicentre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

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

Interventions
Patients will be randomised on entry between:

Arm A:
Cycle I: daunorubicine/cytarabine-arabinoside
Cycle II: intermediate dose cytarabine-arabinoside.

Arm B:
Cycle I: daunorubicine/cytarabine-arabinoside and two doses of bevacizumab 5 or 10 mg/kg
Cycle II: intermediate dose cytarabine-arabinoside and two doses of bevacizumab 5 or 10 mg/kg

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Daunorubicine/cytarabine-arabinoside and bevacizumab

Primary outcome measure
Incidence of Dose-Limiting Toxicity (DLT) and the effect of bevacizumab on the CR-rate.

Secondary outcome measures
1. Overall survival (time from registration until the death of the patient)
2. Event free survival (i.e., time from registration to induction failure, death or relapse whichever occurs first)
3. Minimum Residual Disease (MRD) percentage

Overall study start date
13/02/2007

Completion date
01/10/2008

Eligibility

Key inclusion criteria
1. Patients greater than 60 years
2. Patients eligible for standard chemotherapy
3. Patients with a confirmed diagnosis of Acute Myeloid Leukaemia (AML) French-American-British (FAB) classification M0 - M2 or M4 - M7 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 greater than or equal to 1.5
4. Subjects with secondary AML progressing from antecedent (at least four months duration)

myelodysplasia are also eligible.
5. Serum Glutamic Oxaloacetic Transaminase (SGOT) (Aspartate aminotransferase [AST]) and Serum Glutamic Pyruvic Transaminase (SGPT) (Alanine Aminotransferase [ALT]) less than or equal to 1.5 x the Upper Limit of the Normal range (ULN) at the laboratory where the analyses were performed
6. Total serum bilirubin level less than or equal to 1.5 x the ULN at the laboratory where the analysis was performed
7. Serum creatinine concentration less than or equal to 1.5 x the ULN at the laboratory where the analysis was performed
8. Proteinuria at baseline: urine dipstick of proteinuria less than 2+. Patients discovered to have greater than or equal to 2+ proteinuria on dipstick urinalysis at baseline, should undergo a 24-hour urine collection and must demonstrate less than or equal to 1 g of protein/24 hr
9. World Health Organisation (WHO) performance status less than or equal to two
10. Written informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Not Specified

Target number of participants
200

Key exclusion criteria
1. Patients previously treated for AML (any anti-leukaemic therapy including investigational agents)
2. Past or current history (within the last two years prior to randomisation) of malignancies except for the indication under this study and curatively treated basal and squamous cell carcinoma of the skin or in-situ carcinoma of the cervix
3. Clinically significant (i.e. active) cardiovascular disease, for example cerebrovascular accidents (less than or equal to six months prior to randomisation), myocardial infarction (less than or equal to six months prior to randomisation), unstable angina, New York Heart Association (NYHA) grade II or greater congestive heart failure, serious cardiac arrhythmia requiring medication, reduced left ventricular ejection fraction of less than 50% as evaluated by echocardiogram or Multiple Gated Acquisition (MUGA) scan
4. Uncontrolled hypertension
5. Patients with a history of non-compliance to medical regimens or who are considered unreliable with respect to compliance
6. Patients with any serious concomitant medical condition which could, in the opinion of the investigator, compromise participation in the study
7. Patients who have senile dementia, mental impairment or any other psychiatric disorder that prohibits the patient from understanding and giving informed consent
8. Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to study treatment start, or anticipation of the need for major surgical procedure during the course of the study
9. Serious, non-healing wound, ulcer, or bone fracture
10. Patients with bleeding diathesis or coagulopathy (unless related to AML)

11. Patients with known allergy to Chinese hamster ovary cell proteins or other recombinant human or humanised antibodies or to any excipients of bevacizumab formulation; or to any other study drugs

Date of first enrolment
13/02/2007

Date of final enrolment
01/10/2008

Locations

Countries of recruitment
Netherlands

Study participating centre
VU Medical Centre (VUMC)
Amsterdam
Netherlands
1007 NL

Sponsor information

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

Funder Name
Koningin Wilhelmina Fonds (KWF) (The 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