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An open label randomised controlled study in elderly subjects with previously untreated acute myelogenous leukaemia, comparing treatment groups randomised to receive daunorubicin and cytarabine or daunorubicin, cytarabine and PSC-833

Submission date 19/12/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/12/2005	**Overall study status** Completed	
Last Edited 13/11/2008	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
HO31; NTR360

Study information

Scientific Title

Acronym
HOVON 31 AML/Novartis PSC C 302-E-00

Study objectives
Evaluation of the effect of PSC-833 during induction treatment with daunorubicin and cytarabine.

Ethics approval required
Old ethics approval format

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

Study design
Multicentre, open label, randomised, active controlled, parallel group study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute myeloid leukaemia (AML)

Interventions
Patients with AML, meeting all eligibility criteria will be randomised on entry between:
Arm A: two induction cycles of daunorubicin (DNR) 45 mg/m^2/day, days 1 - 3 and cytarabine (Ara-C) 200 mg/m^2/day, days 1 - 7, or
Arm B: two induction cycles of DNR 35 mg/m^2/day, days 1 - 3; Ara-C 200 mg/m^2/day, days 1 - 7; and PSC-833 loading dose 2 mg/kg over 2 hours, followed by 10 mg/kg/day, days 1 - 3

Patients in CR will then be given one consolidation cycle without PSC-833 consisting of Ara-C, mitoxantrone and etoposide.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)

Daunorubicin, cytarabine, PSC-833

Primary outcome(s)
Event-free survival

Key secondary outcome(s))
1. Complete remission
2. Disease-free survival
3. Overall survival
4. Association between complete remission and expression of P-gp by AML-blasts

Completion date
17/02/1999

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 60 years
2. Subjects who have a cytopathologically confirmed diagnosis of previously untreated AML (M0-M2 and M4-M7, FAB classification)
3. Subjects with secondary AML progressing from antecedent MDS are eligible if there has been no previous chemotherapy. Antecedent MDS is defined as any antecedent haematological disease of at least 4 months duration.
4. World Health Organization (WHO) performance status less than or equal to 2
5. Subjects have given written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
1. Cytopathologically confirmed central nervous system (CNS) infiltration. NB: in the absence of clinical suspicion of CNS involvement, lumbar puncture is not required.
2. Subjects have had previous Polycythemia Rubra Vera, primary myelofibrosis, are in blast cell crisis of chronic myeloid leukaemia or are M3 AML according to FAB classification
3. Subject has neurosensory toxicity greater than or equal to Grade 2 (NCIC Expanded CTC)
4. Subject has neurocerebellar toxicity greater than or equal to Grade 1 (NCIC Expanded CTC)
5. Subject is known to be positive for human immunodeficiency virus (HIV) type 1 antibody (testing to determine HIV antibody status is not necessary to be eligible)
6. Subject has impairment of hepatic or renal function as defined by the following baseline laboratory values:
6.1. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) greater than or

equal to 2.5 times IULN
6.2. Alkaline phosphatase greater than or equal to 2.5 times IULN
6.3. Serum total bilirubin greater than or equal to 1.5 times IULN
6.4. Serum creatinine greater than or equal to 1.5 times IULN after adequate hydration
7. Subject is currently receiving treatment with any of the agents listed in the protocol if treatment cannot be discontinued at the specified time relative to PSC-833 administration. All of the drugs listed are well substantiated to interact with cyclosporin A.
8. Subject has had major surgery within 2 weeks of study entry
9. Subject has received investigational therapy within 30 days of study entry
10. Subject has known hypersensitivity to cyclosporin A
11. Subject has received prior radiotherapy within 4 weeks of study entry
12. Subject is less than 5 years free of another primary malignancy with the exception of basal cell carcinoma of the skin and stage 1 cervical carcinoma
13. Subject has previously been treated with chemotherapy for AML
14. Subject has concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension etc.)
15. Subject has a psychological, intellectual or sensory dysfunction which is likely to impede their ability to understand and comply with study requirements
16. Subject had a myocardial infarction within the last 6 months, has symptomatic ischaemic heart disease, congestive heart failure or other uncontrolled coronary disease

Date of first enrolment
12/05/1997

Date of final enrolment
17/02/1999

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Center
Rotterdam
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Sponsor information

Organisation
Novartis Pharma AG (Switzerland)

ROR
https://ror.org/02f9zrr09

Funder(s)

Funder type
Research organisation

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

Funder Name
Novartis Pharma B.V. (The Netherlands)

Results and Publications

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	15/10/2005		Yes	No