Randomized maintenance therapy with Azacitidine (Vidaza) in older patients (>= 60 years of age) with acute myeloid leukemia (AML) and refractory anemia with excess of blasts (RAEB, RAEB-t)

Published: 20-02-2009
Last updated: 06-05-2024

- To assess, in a randomized study the value of Azacitidine as post remission therapy (in comparison to observation) in elderly patients with AML, RAEB or RAEB-t with respect to the disease free survival.- In addition, post remission Azacitidine...

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

Summary

ID

NL-OMON37945

Source
ToetsingOnline

Brief title
HOVON 97 AML

Condition

- Leukaemias

Synonym
Acute myeloid leukemia, leukemia

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: Celgene Corporation,Stichting HOVON;KWF

Intervention

Keyword: acute myeloid leukemia, Azacitidine, maintenance, refractory anemia

Outcome measures

Primary outcome

- Disease-free survival measured from the date of randomization to relapse or

death from any cause whichever comes first.

Secondary outcome

- Overall survival measured from the date of randomization

- Probability of relapse and death after inclusion from date of randomization

calculated as competing risks.

- Number and duration of hospitalization as well as transfusion requirements

(red cell and platelet transfusion).

- Adverse events

Study description

Background summary

For elderly patients newly diagnosed with AML attaining CR, post-remission chemotherapy consisting of high dose cytarabine has not provided significant benefits due to enhanced toxicity. Marrow ablative cytotoxic stem cell transplants are rarely applied in patients with AML of 60 yrs and older for similar reasons. As a consequence, other avenues need to be pursued to prevent relapse in complete responders of older age.
Recent studies have suggested that maintenance chemotherapy applied for several months during remission in older patients with AML may reduce the frequency of relapse

Morphologic (dysplasia) and cytogenetic criteria present in malignant blast cells of elderly patients, suggest that AML and Myelodysplastic Syndromes (MDS) might be associated diseases. It could be argued that elderly patients with AML, who have less than 5% blasts in their bone marrow after intensive chemotherapy, still have a disease comparable with MDS. These facts and the efficacy of Azacitidine in MDS argue for the use of Azacitidine as maintenance therapy after 2 cycles of intensive chemotherapy in patients with AML, obviously at high risk of relapse.

Study objective

- To assess, in a randomized study the value of Azacitidine as post remission therapy (in comparison to observation) in elderly patients with AML, RAEB or RAEB-t with respect to the disease free survival.
- In addition, post remission Azacitidine therapy will be evaluated with respect to toxicity, probability of relapse and probability of death in first CR and overall survival.
- To evaluate prognostic factors (e.g. phenotype, cytogenetics) in the context of post remission therapy with Azacitidine as regards to overall survival, and disease free survival.

Study design

Prospective, multicenter, randomized phase III trial.

Intervention

maintenance therapy with Azacitidine or observation

Study burden and risks

The most common adverse effects of Azacitidine are myelosuppression, nausea and vomiting and injection site reactions.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age 60 years or more
- Subjects with a cytopathologically confirmed diagnosis of
(a) AML (M0-M2 and M4-M7, FAB classification)or
(b) refractory anemia with excess of blasts (RAEB) or refractory anemia with excess of blasts in transformation (RAEB-t) with an IPSS score of >1.5
Note: Subjects with a secondary AML progressing from antecedent myelodysplasia and biphenotypic leukaemia are eligible.
- Less than 5% bone marrow blasts and absence of Auer rods after 2 cycles of induction therapy
- Hematological recovery, i.e. ANC >= 0.5 x 109/l and platelets >= 50 x 109/l
- WHO performance status <= 2
- Written informed consent

Exclusion criteria

- Extramedullary disease
- Planned allogeneic hematopoietic cell transplantation
- Previous polycythaemia rubra vera
- Primary myelofibrosis
- Blast crisis of chronic myeloid leukemia
- AML-FAB type M3 or AML with cytogenetic abnormality t(15;17)
- Impaired hepatic or renal function as defined by:
ALT and/or AST > 2.5 x normal value

Bilirubin > 2 x normal value
Serum creatinin > 2 x normal value (after adequate hydration)
- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.)
- Cardiac dysfunction as defined by:
Myocardial infarction within the last 6 months of study entry, or
Reduced left ventricular function with an ejection fraction <50%
Unstable angina
Unstable cardiac arrhythmias

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-06-2009
Enrollment:	86
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Vidaza
Generic name:	Azacitidine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-02-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-03-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2013

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-01-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-11-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-001290-15-NL
CCMO	NL23888.042.08