Decitabine-cytarabine chemotherapy in elderly AML and high risk MDS patients (> 65 years) with high early mortality risk

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Primary objectives:• To assess early mortality risk (first 30 days after start of induction therapy) of treatment with decitabine-cytarabine in elderly patients with AML or high risk myelodysplastic syndrome (IPSS >=1.5) with a high risk of early…

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

Summary

ID

NL-OMON42455

Source
ToetsingOnline

Brief title
LUMC2015-02: Decitabine-cytarabine

Condition

- Leukaemias

Synonym
acute leukemia, myelodysplasia

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: AML, cytarabine, decitabine, high risk MDS

Outcome measures

Primary outcome

• Day 30 mortality

Secondary outcome

• Remission status after one cycle of decitabine-cytarabine

• Remission status after two cycles of decitabine-cytarabine

Study description

Background summary

Although considerable progress has been made the last decades in the treatment of acute myeloid leukemia (AML), treatment of elderly patients (>= 60 years) still remains a challenge. With standard induction chemotherapy no more than 50-60% of patients achieve a complete remission. When using only chemotherapy treatment, long-term survival is poor due to high relapse rates.
However, cure is possible in elderly patients with AML using the immunotherapeutic potential of allogeneic stem cell transplantation (alloSCT). Non-myeloablative (NMA) or reduced intensity conditioning (RIC) regimens have been developed which can be used in patients up to 75 years of age with long term overall survival of 40-50% (2, 3).
One of the major problems in elderly patients is early mortality during induction chemotherpay. Early mortality has been defined as death occurring within the first month (or 30 days) after the start of induction chemotherapy.
In the last four decades the early mortality rate has dropped significantly from 18.7% to 5.8% in younger patients with AML (< 65 years). In patients over 65 years early death rates remain high, ranging from 10-20%, and becoming even higher in patients over 75 years (20-40%).
High early mortality rates are especially observed in patients with co-morbidity. In our own center we have observed an early mortality rate of 37.5% in AML patients over 65 year with a HCT co-morbidity index value of >=2. In AML patients over 65 years without or with low co-morbidity (HCT co-morbidity index value of 0 or 1) iearly mortality rate was 7-8%.

A promising new therapeutic option is treatment with sequential decitabine-cytarabine, which showed no early mortality in a very old AML patient group with a median performance score of 1. This regimen also resulted in an impressive CR rate of 70%.
In this study we want to treat AML patients over 65 years with a HCT co-morbidity index of 2 and higher with sequential decitabine-intermediate dose cytarabine. The aim of this study is to reach an early mortality rate of less than 10%.

Study objective

Primary objectives:
• To assess early mortality risk (first 30 days after start of induction therapy) of treatment with decitabine-cytarabine in elderly patients with AML or high risk myelodysplastic syndrome (IPSS >=1.5) with a high risk of early mortality (HCT-CI score >=2)

Secondary objectives:
• To evaluate remission status after one and two cycles of decitabine-cytarabine

Study design

Phase 1-2 interventional study

Intervention

Patients will receive decitabine one time daily 20 mg/m2 during 5 days, directly followed by cytarabine 100 mg/m2 per day as continuous infusion during 5 days. At day 28-35 after the start of chemotherapy, remission status will be determined. In case of complete remission, complete remission with incomplete recovery or morphologic leukemia-free state, patients will receive a second cycle of decitabine-cytarabine. At day 28-35 after the start of the second cycle, remission status will be determined.

Study burden and risks

Elderly patients with AML or high risk MDS (>=60 years) have a poor prognosis, without treatment most patients die within weeks. With supportive care using antibiotics and regular blood transfusions survival can be extended by weeks, or a few months in a small subset of patients. Intensive chemotherapy can induce complete remissions in 40-60% of patients, resulting in a return to normal life for many months or even more than a year. Patients in complete remission can also decide to undergo allogeneic stem cell transplantation with the possibility of cure from the disease.
Induction chemotherapy is complicated by morbidity and early mortality, which

occurs mainly in the first month of treatment. However, mortality in patients undergoing intensive chemotherapy is always lower than mortality occurring in patients on supportive care.
Early mortality is especially high in patients aged over 65 years with co-morbidity. These patients should not be treated with standard induction chemotherapy. Because the decitabine-cytarabine treatment in this protocol is less intensive than standard chemotherapy it is to be expected that participation within this protocol will result in a high likelihood of achieving a complete remission with a limited chance of early mortality. Patients up to 75 years that achieve complete remission with this protocol will next be offered allogeneic stem cell transplantation with the possibility of cure.

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

- patients with AML or high risk MDS (IPSS-R >= 4.5)
- > 65 years
- WHO performance score 0-2
- HCT-CI score >=2
- Written informed consent

Exclusion criteria

- Previous treatment with decitabine, azacitidine or intensive chemotherapy for this MDS/AML (treatment with chemotherapy for previous other diseases is acceptable)
- Acute promyelocytic leukemia

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-04-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cytarabine
Generic name:	Cytarabine

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dacogen
Generic name:	Decitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-11-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-11-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2015-004896-60-NL
CCMO	NL54494.058.15

Study results

Date completed:	10-12-2019
Actual enrolment:	19