International multicenter, open-label, phase 2 study to treat molecular relapse of pediatric acute myeloid leukemia with azacitidine

Published: 05-11-2018
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• Primary Objective: To evaluate the effect of azacitidine treatment in AML subjects at molecular relapse after CR1 with regard to molecular response prior to further treatment (reinduction / HSCT)• Secondary Objectives:o To assess safety of…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON52770

Source
ToetsingOnline

Brief title
AMoRe2017

Condition

- Leukaemias

Synonym
Acute myeloid leukemia, AML

Research involving
Human

Sponsors and support

Primary sponsor: German Pediatric Oncology Group

Source(s) of monetary or material Support: Celgene Corporation,Farmaceutische industrie;zie G2 en GPOH

Intervention

Keyword: acute myeloid leukemia, azacitdine, children, molecular relapse

Outcome measures

Primary outcome

The primary endpoint based on molecular response will be assessed at the end of

the azacitidine treatment.

Secondary outcome

• Toxicities

• Event-free-survival

• Disease free survival

• Overall-survival

• Quality of life

Study description

Background summary

The majority of patients with newly diagnosed AML achieve a CR after induction chemotherapy. However, relapse occurs in about one-third of children and far fewer achieve CR after reinduction chemotherapy. The probability of survival at 4 years is 38% in the most recent study of relapsed AML patients (Kaspers, 2013), which is consistent with earlier studies showing survival rates around 30%. Failure to achieve CR after reinduction is associated with failure of subsequent attempts at curative therapy such as HSCT. Further improvements of current treatment, including improvements in remission induction for relapsed patients are thus required.

Study objective

• Primary Objective: To evaluate the effect of azacitidine treatment in AML

subjects at molecular relapse after CR1 with regard to molecular response prior to further treatment (reinduction / HSCT)

• Secondary Objectives:
o To assess safety of azacitidine treatment in children and adolescents with a molecular relapse of AML
o Disease free and overall survival post molecular relapse
o Quality of life (questionnaire, AE reports).

Study design

Prospective, multi-center, open label, phase 2 trial

Intervention

Intravenous azacitidine 75 mg/m2, Days 1 to 7 of a 28-day cycle for up to 3 cycles initially.
In case of decline of MRD during azacitidine treatment additional cycles are allowed (maximum 6 cycles).

Study burden and risks

Possible adverse events of this study are:
• anemia,
• low number of white blood cells with or without fever
• infections, inlcuding pulmonary infection or urinary tract infection
• nausea
• vomiting
• diarhea
• pain in the stomach
• constipation
• tired, unwel or feeling weak
• sore throat
• less appetite
• pain
• dizziness
• shortness of breath with or whithout exercise
• skin rash
• itching
• bruising
• response to place of injection

Contacts

Public
German Pediatric Oncology Group

Hufelandstrasse 17
Essen 45147
DE
Scientific
German Pediatric Oncology Group

Hufelandstrasse 17
Essen 45147
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

1. Aged 3 months to <21 years with documented diagnosis of AML according to WHO classification with at least one quantitative genetic maker, e.g. one of the following
aberrations:
• t(8;21); RUNX1-RUNX1T1
• inv(16); CBFb-MYH11
• t(9;11); MLL-AF9
• t(10;11); MLL-AF10
• NPM1

• FLT3-ITD
• WT1; etc.
2. First complete remission (MRD in PB less than 5 x 10-4) confirmed at the start of last
consolidation course or within 1 month after completion of consolidation treatment
3. Detection of a confirmed molecular relapse of an AML
4. Understand and voluntarily provide permission (subjects and when applicable, parental/legal representative(s)) to the ICF prior to conducting any study related
assessments/procedures
5. Able to adhere to the study visit schedule and other protocol requirements
6. Lansky performance score at least equal to 50; or Karnofsky performance status at
least equal to 50, whichever is applicable
7. Negative serum pregnancy tests for females of child bearing potential within 10 days
prior to treatment

Exclusion criteria

1. Concomitant treatment with any other anticancer therapy except those specified in
protocol
2. HSCT within previous 3 months
3. Treated by any investigational agent in a clinical study within previous 4 weeks
4. Pregnancy or lactating
5. FAB type M3 leukemia (acute promyelocytic leukemia)
6. Therapy-related AML
7. AML of Down syndrome or other congenital syndromes giving rise to leukemia or treatment complications
8. Symptomatic cardiac disorders (CTCAE 4.0 Grade 3 or 4)
9. Evidence of invasive fungal infection or other severe systemic infection requiring
treatment doses of systemic/parenteral therapy including known active viral infection
with human immunodeficiency virus (HIV) or Hepatitis Type B and C
10. Any other organ dysfunction (CTCAE 4.0 Grade 3 or 4) that will interfere with the
administration of the therapy according to this protocol
11. Ongoing severe toxicities (CTCAE 4.0 Grade 3 or 4) of prior chemotherapy/stem cell
transplantation
12. Hypersensitivity to the active substance or other excipients contained in

the
investigational medical product listed in the summary of product characteristics (SmPC)
or Investigators Brochure (IB).
13. Abnormal liver function:
a. serum bilirubin > 3 x ULN or
b. ALT or AST > 5 times ULN
14. Symptomatic CNS-involvement or isolated extramedullary disease at initial diagnosis
15. Female and male subjects with child bearing potential who avoid using highly effective
anticonceptive measure(ment)s

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-06-2020
Enrollment:	6
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	05-11-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-02-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
Other	DRKS00015449
EudraCT	EUCTR2017-003422-32-NL
CCMO	NL66579.078.18