A Phase 2, multicenter, open-label study to evaluate the pharmacokinetics, pharmacodynamics, safety and activity of azacitidine and to compare azacitidine to historical controls in pediatric subjects with newly diagnosed advanced myelodysplastic syndrome or juvenile myelomonocytic leukemia before hematopoietic stem cell transplantation

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

Summary

ID

NL-OMON41785

Source
ToetsingOnline

Brief title
AZA-JMML-001

Condition

- Leukaemias

Synonym
juvenile chronic myeloid leukemia, myelodysplasia

Research involving
Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: azacitidine, hematopoietic stem cell transplantation, juvenile myelomonocytic leukemia, myelodysplastic syndrome

Outcome measures

Primary outcome

Response Rate at Cycle 3 Day 28

Secondary outcome

- Cytogenetic Response for MDS subjects; Cytogenetic and Molecular Response for

JMML subjects

- Duration of response

- Time to response

- Time to progression

- Leukemia free survival

- Overall survival

- Deoxyribonucleic acid methylation status in BM on Days 1 and 15 of Cycle 1,

Day 28 of Cycle 3, pre-HSCT, and at the time of relapse/progression

- Percentage of subjects undergoing HSCT

- Time to first HSCT

-Safety defined by frequency and severity of treatment emergent AEs

- Pharmacokinetics

Study description

Background summary

Based on the available adult and pediatric data, azacitidine seems to be a very promising
treatment option for pediatric advanced MDS and JMML. In addition to the clinical response
rates outlined above, cytogenetic and molecular responses have also been observed with the use
of azacitidine, unlike the responses seen with current therapeutic agents, which provide more
moderate response with increased toxicity. This further supports the value of studying
azacitidine given prior to HSCT in MDS/JMML and the potential benefit of giving azacitidine in
this patient population.

Study objective

The primary objective is to assess the treatment effect on response rate (MDS: either complete
remission [CR], partial remission [PR], or marrow CR; JMML: either clinical complete
remission [cCR] or clinical partial remission [cPR]); at Cycle 3 Day 28 and to compare against
standard therapy using a matched-pairs analysis of historical data.

Study design

This is a prospective, open-label, Phase 2 study consisting of 2 parallel experimental arms, one
for each disease group: MDS and JMML.
Twenty subjects with MDS and 35 JMML subjects evaluable for the primary endpoint (ie,
subjects that receive at least 1 dose of investigational product [IP]) will be

enrolled at
approximately 45 centers in Europe. If, during Stage 1 evaluation, less than 2 subjects are
observed with a CR, PR, or marrow CR after 3 cycles of azacitidine in the first 9 subjects with
MDS, then enrollment will be stopped. Similarly, if less than 3 subjects are observed with a cPR
or cCR after 3 cycles of azacitidine in the first 18 subjects with JMML, then enrollment will be
stopped.

Intervention

Azacitidine 75 mg/m2, either IV or SC, will be administered QD on Days 1 to 7 of a 28-day
cycle for a minimum of 3 cycles and a maximum of 6 cycles, provided that the subject does not
have disease progression (based on an independent central review of responses - see above under
Study Design) or HSCT from Cycles 4 through 6.

Study burden and risks

Please refer to the table of evens in the protocol for a complete overview of the procedures.

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cycle for a minimum of 3 cycles and a maximum of 6 cycles, provided that the subject does not
have disease progression (based on an independent central review of responses - see above under
Study Design) or HSCT from Cycles 4 through 6.

Risks associated with participation in this study are the normal risks of pediatric oncology treatments.

Possible side effects of Vidaza:
• anemia
• low number white blood cells with or without fever
• decrease in number of platelets
• Infections, including pulmonary infection or urinary tract infection
• nausea
• vomiting
• diarrhea
• pain in the stomach

• constipation
• tired, unwell, or weak fealing
• sore throat
• less appetite
• pain
• dizziness
• shortness of breath with or without exercise
• skin rash
• itching
• bruise
• response to place of injection

Contacts

Public
Celgene Corporation

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New Jersey 07901
US
Scientific
Celgene Corporation

Morris Avenue 86
New Jersey 07901
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

MDS:
1. Patient has newly diagnosed advanced primary or secondary MDS with immature cells in blood or bone marrow or chromosomal abnormality linked to secondary MDS. Blood and bone marrow samples confirming diagnosis within 14 days prior to ICF as for the MDS.
JMML:
1. Patient has newly diagnosed JMML, with samples from blood and bone marrow confirming diagnosis and specific genetic changes.;Both MDS and JMML:
2.Patient has a Lansky play score/ Karnofsky performance status at least equal to 60
3.Patient has a normal renal function and a normal liver function.
4.Subjects should be between 1 month to less than 18 years at time of signing ICF/ IAF

Exclusion criteria

MDS exclusions:
1.Patient has an illness caused by 'germline genetic defects'.
2.Patient has inherited bone marrow failure syndrome.
JMML exclusion:
1.Patient has germline genetic defects.
Both:
1.Patient has organ dysfunction that will interfere with the administration of the therapy according to this protocol.
2.Hypersensitivity to azacitidine

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-06-2016
Enrollment:	2
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:	27-03-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-09-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	25-03-2019
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
EudraCT	EUCTR2014-002388-13-NL
CCMO	NL50476.078.15

Study results

Results posted: 11-11-2019

First publication
28-10-2019