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

Published: 27-03-2015 Last updated: 13-04-2024

The primary objective is to assess the treatment effect on response rate (MDS: either completeremission [CR], partial remission [PR], or marrow CR; JMML: either clinical completeremission [cCR] or clinical partial remission [cPR]); at Cycle 3 Day 28...

Ethical reviewApproved WMOStatusRecruitingHealth condition typeLeukaemiasStudy typeInterventional

# 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

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- 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

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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

Morris Avenue 86 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. IMML:
- 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.

### **IMML** 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