A phase II/III randomized, open-label study to compare the efficacy and safety of intravenous volasertib in combination with subcutaneous cytarabine versus investigator*s choice of anti-leukemic treatment in adult patients with relapsed or refractory acute myeloid leukemia with no established treatment options (POLO-AML 1)

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To investigate the efficacy, safety, and pharmacokinetics of volasertib in combination with low-dose cytarabine versus investigator*s choice of anti-leukemic treatment in patients with relapsed or refractory acute myeloid leukemia with no...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON36189

Source
ToetsingOnline

Brief title
POLO-AML 1

Condition

- Leukaemias
- Leukaemias

Synonym
Acute myeloid leukemia, leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim bv

Intervention

Keyword: Acute myeloid leukemia, efficacy, Polo-like kinase, safety

Outcome measures

Primary outcome

Phase II part: percentage complete remission (CR)

Phase III part: Overall Survival (OS)

Secondary outcome

Event free survival (EFS)

Complete Remission with incomplete blood count recovery (CRi)

Relapse Free Survival (RFS)

Remission duration

Study description

Background summary

Acute myeloid leukemia (AML) is the most common malignant myeloid disorder in adults. AML is characterized by uncontrolled growth of immature bone marrow

cells, leading to impaired production of normal blood cells. Symptoms are caused by the decrease in the number of normal blood cells. Without therapeutic intervention, the disease progresses and leads to death within months after initial diagnosis. In the majority of patients with AML who achieve a complete remission after initial therapy the leukemia will recur within 3 years after diagnosis. Patients with recurrent or refractory AML have a worse prognosis, especially if they are not eligible for intensive treatment. For this group of patients, no established treatment options are available. Volasertib is an inhibitor of polo-like kinase 1 (PLK1), a target that is overexpressed in various human cancers. Published preclinical and clinical data suggest that PLK1 is a potential target for the treatment of AML. Clinical trials with volasertib have shown that this drug has an acceptable safety profile. Volasertib in combination with low-dose cytarabine shows preliminary anti-leukemia activity, suggesting that this therapy is effective in patients with relapsed/refractory AML. Therefore, this study has been designed to further test the efficacy of this combination.

Study objective

To investigate the efficacy, safety, and pharmacokinetics of volasertib in combination with low-dose cytarabine versus investigator*s choice of anti-leukemic treatment in patients with relapsed or refractory acute myeloid leukemia with no established treatment options.

Study design

Phase II/III, randomized, active-controlled, open-label, parallel group comparison.
A total of 450 patients will be randomized in a 1:1 ratio to received treatment in Arm A or Arm B. An interim analysis will be performed at the end of the phase II part of the study. The phase II part is completed when 300 patients have been enrolled and treated for at least 4 cycles or discontinued/dropped out of the trial. When complete remission (CR, see below) shows statistical significance, further patients will be enrolled into the phase III of the study.

Intervention

Arm A: intravenous volasertib 350 mg every two weeks and subcutaneous low-dose cytarabine injections twice daily on days 1-10 of a 28-day cycle.

Arm B: investigator choice of the most appropriate anti-leukemic treatment available in the local market

Study burden and risks

This study investigates the efficacy and safety of the combination of volasertib and cytarabine in patients with relapsed/refractory AML who are not eligible to receive intensive treatment. The expected adverse events are: neutropenia, leukopenia, thrombocytopenia, anemia, gastro-intestinal disorders, alopecia. These adverse events can be monitored well and supportive treatment is available.
Patients will undergo repeated blood samplings for safety and disease assessment, recording of vital signs, and bone marrow examinations, which would be performed regardless of participation in this study. However, the frequency of these procedures may be higher than usual.
Additional blood samplings will be performed for pharmacokinetic analyses. A single blood draw may be performed for an optional pharmacogenetic test during the first cycle. The patient may refuse participation in this sampling, but can continue to participate in the main study. These procedures can lead to local pain, bruising, irritation, or an infection in rare cases.

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

Adults with relapsed or refractory AML, considered not to benefit from / not to be eligible for standard intensive therapy and / or stem cell transplantation based on one of the following criteria:
a. AML patient 60 years of age or older failing to achieve complete remission after standard induction
b. Relapsed AML patient 60 years of age or older and at least one of the following:
- first complete remission duration <18 months.
- previous allogeneic stem cell transplant.
- adverse cytogenetics and/or molecular genetics.
- more than 1st relapse.
c. AML patient <60 years of age failing to achieve complete remission after induction.
d. Relapsed AML patient <60 years of age who has already received high-dose cytarabine salvage and/or allogeneic stem cell transplant.

Exclusion criteria

- Previously untreated AML
- Acute promyelocytic leukemia
- Second malignancy currently requiring active therapy
- Current symptomatic leukemic CNS involvement.
- Clinically relevant QTcF prolongation
- Severe illness or organ dysfunction involving the heart, kidney, liver or other organ system
- Concomitant anti-leukemic treatment.
- Concomitant anti-infective therapy
- Uncontrolled systemic fungal, bacterial, viral, or other infection
- Female patients of childbearing potential who are sexually active and unwilling to use a medically acceptable method of contraception during the trial
- Pregnancy or breast feeding
- Recent treatment with any investigational drug

Study design

Design

Study phase:	2
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	11
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Ara-cell
Generic name:	cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	not yet known
Generic name:	volasertib

Ethics review

Approved WMO

Date:	10-06-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	16-09-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2010-023499-25-NL
CCMO	NL36814.029.11