A phase III randomised, double-blind, controlled, parallel group study of intravenous volasertib in combination with subcutaneous low-dose cytarabine vs. placebo + low-dose cytarabine in patients * 65 years with previously untreated acute myeloid leukaemia, who are ineligible for intensive remission induction therapy

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

Summary

ID

NL-OMON41320

Source
ToetsingOnline

Brief title
POLO-AML 2

Condition

- Leukaemias

Synonym
Acyte Myeloid Leucemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AML, cytarabine, volasertib

Outcome measures

Primary outcome

Primary endpoint: Complete Remission (CR) and Complete Remission with

incomplete blood count recovery (CRi), based on blinded central review

Secondary outcome

Key secondary endpoint: Overall Survival (OS).

Secondary endpoints: Event-Free Survival (EFS), Relapse-Free Survival (RFS).

Remission duration, quality of life (QoL) measured by EQ-5D 5L and FACT-Leu,

pharmacogenomics, biomarker analyses, pharmacokinetics of volasertib when given

in combination with cytarabine, Health Care Resources Utilization (HCRU

Study description

Background summary

Acute Myeloid Leukaemia also called AML is a cancer of the blood and bone

marrow, characterized by a rapid, uncontrolled growth of abnormal white blood cells. When leukaemic cells accumulate in the bone marrow, there is less room for healthy white blood cells, red blood cells, and platelets. Due to the reduction of normal blood cells, infection, anaemia, or easy bleeding may occur. The leukaemic cells can spread outside the blood to other parts of the body.

The incidence of AML increases with age : the median age of diagnosis is 63 years
Elderly patients, as aimed for in this study, have very few therapeutic options : often they are treated with low dose cytarabine of theyare offered best supportive care, seen they often are not eligible for intensive therapy.

Volasertib*s effect has been shown to occur via inhibition of an important protein called Polo-Like Kinase 1 (PLK1), which is necessary for leukaemic cell multiplication. Volasertib inhibits the normal functioning of these proteins by fixing itself on them, which inhibits the growth of leukaemic cells. Since PLK1 is also present in normal, healthy tissue, volasertib can also adversely affect healthy tissues and organs of the body where cell division occurs.

Study objective

To investigate the efficacy, safety, and pharmacokinetics of intravenous volasertib + subcutaneous low-dose cytarabine in patients * 65 years of age with previously untreated acute myeloid leukaemia, ineligible for intensive remission induction therapy.
Besides this, the concentration and pharmacokinetics, the safety and possible side effects and teh quality of life will be investigated.
As part of routine practice for the diagnose of AML, the genetics of the leucemic cells will be investigated, and this before, during and after the treatment (cytogenitical, molecular-genetic and morphological assessment).
The treatment will be stopped in case the patient dies, or when in the investigator's opinion, no more benefit is expected of the study treatment.

Study design

Phase III, randomised, double-blind, parallel group study

Intervention

Arm A : volasertib + low dose cytarabine
Arm B : volasertib placebo + low dose cytarabine

Study burden and risks

At screening the patient will undergo a physical examination, ECG, blood and

bone marrow samples.
During the 1st cycle, the patient will need to come 5x to the hospital
During the subsequent cycles, the patient will need to come 3x to the hospital

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

Age * 65years.
Cytologically/histologically confirmed AML according to WHO classification [R09-2581]; (except for acute promyelocytic leukaemia (APL)).
Previously untreated AML (except for hydroxyurea and/or corticosteroid therapy for no more than 28 days (cumulative)). Previous therapy for MDS is allowed.
Investigator considers patient ineligible for intensive remission induction therapy based on documented medical reasons (e.g. disease characteristics like AML genetics, type of AML (de

novo or secondary), and patient characteristics like performance score, concomitant diagnoses, organ dysfunctions).
Patient is eligible for LDAC treatment.
Eastern Cooperative Oncology Group (ECOG) performance score * 2 at screening.
Signed and dated written informed consent by start date of Screening visit in accordance with GCP and local legislation

Exclusion criteria

1. Prior or concomitant chemotherapy for AML (with the exception of hydroxyurea and/or corticosteroid therapy for no more than 28 days (cumulative)). Please note that any prior therapy for MDS is allowed.
2. Treatment with any investigational drug within 2 weeks before first administration of present trial drug.
3. Acute promyelocytic leukaemia (French-American-British (FAB) classification subtype M3).
4. Current clinical central nervous system (CNS) symptoms deemed by the investigator to be related to leukaemic CNS involvement (no lumbar puncture required, clinical assessment per investigator*s judgement is sufficient).
5. Hypersensitivity to one of the trial drugs or the excipients.
6. Severe illness or organ dysfunction involving the heart, kidney, liver or other organ system (e.g. active infection, clinically relevant impairment of cardiac function, severe heart failure/cardiac insufficiency, unstable angina pectoris or history of recent myocardial infarction), which in the opinion of the investigator precludes treatment with LDAC.
7. QTcF prolongation > 470 ms or QT prolongation deemed clinically relevant by the investigator (e.g., congenital long QT syndrome).The QTcF will be calculated as the mean of the 3 ECGs taken at screening.
8. Total bilirubin > 3 x ULN.
9. Creatinine clearance (CLcr) < 30 ml/min (estimated creatinine clearance by the Cockcroft-Gault (C-G) equation (see Appendix 10.2 for the formula).
10. Active hepatitis B or hepatitis C, or laboratory evidence for a chronic infection.
11. HIV infection.
12. Second malignancy currently requiring active therapy (except for hormonal/anti-hormonal treatment, e.g. in prostate or breast cancer).
13. Any significant concurrent psychiatric disorder or social situation that according to the investigator*s judgement would compromise patient*s safety or compliance, interfere with consent, study participation, or interpretation of study results.
14. Known or suspected active alcohol or drug abuse.
15. Patient unable to comply with the protocol, in the opinion of the investigator.
16. Male patients with partners of childbearing potential who are unwilling to use condoms in combination with a second medically acceptable method of contraception during the trial and for a minimum of 6 months after study treatment

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-08-2013
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ARA-Cell
Generic name:	cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA
Generic name:	volasertib

Ethics review

Approved WMO

Date:	21-02-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	18-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	16-08-2016
Application type:	Amendment
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	EUCTR2012-002487-27-NL
CCMO	NL42278.029.13