A randomized Phase III study to compare arsenic trioxide (ATO) combined to ATRA and idarubicin versus standard ATRA and anthracycLines-based chemotherapy (AIDA regimen) for patients with newly diagnosed, high-risk acute prOmyelocytic leukemia.

Published: 13-06-2017
Last updated: 30-01-2025

To compare event-free survival (EFS) of the experimental treatment arm including ATO/ATRA and idarubicin with standard treatment based on ATRA plus chemotherapy (AIDA regimen).

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

Summary

ID

NL-OMON47163

Source
ToetsingOnline

Brief title
HOVON 138 AML / APOLLO

Condition

- Leukaemias

Synonym
acute promyelocytic leukemia, APL

Research involving
Human

Sponsors and support

Primary sponsor: Technische Universität Dresden
Source(s) of monetary or material Support: Stichting HOVON,TEVA Pharma

Intervention

Keyword: arsenic, leukemia, promyelocytic, trioxide

Outcome measures

Primary outcome

Event-free survival

Secondary outcome

-Rate of hematological CR after induction

-Rate of early death during induction

-Rate of overall survival (OS) at 2 years

-Rate of cumulative incidence of secondary MDS or AML

-Rate of cumulative incidence of relapse (CIR) at 2 years

-Incidence of hematological and non-hematological toxicity

-Rate of molecular remission after last consolidation cycle

-Assessment of PML/RARA transcript level reduction during treatment

-To investigate differences in the following a priori Quality of Life selected

scales: physical and cognitive functioning as well as fatigue, nausea and

vomiting, constipation and appetite loss

-To investigate differences in the immune reconstitution between the two arms

-Total hospitalization days during therapy and health economic impact

Study description

Background summary

Acute promyelocytic leukemia (APL) is a rare subtype of acute myeloid leukemia (AML) characterized by consistent clinical, morphologic, and genetic features. APL is often clinically characterized by the presence of coagulation abnormalities, including disseminated intra vascular coagulation (DIC), hyperfibrinolysis and unspecific proteolysis. Despite the dramatic progress achieved in frontline therapy of APL with ATRA plus anthracycline-based regimens (AIDA), relapses still occur in approximately 20% of the patients. Moreover, these regimens are associated with significant toxicities due to severe myelosuppression frequently associated with life-threatening infections and potentially serious late effects including development of secondary MDS/AML. A combination of ATO with ATRA shows better survival with significant lower toxicity rates compared to standard therapy in low/intermediate risk APL patients. In this trial we intend to perform a trial in high-risk APL patients comparing standard AIDA based treatment with ATO/ATRA combination with low-doses idarubicine during induction. We expect less severe toxicity and treatment-related mortality resulting in an improved outcome for patients in the experimental arm. Furthermore, from the start of consolidation, these patients (in contrast to the standard arm) can be treated on an outpatient basis, which is also considered to be associated with an improved QoL.

Study objective

To compare event-free survival (EFS) of the experimental treatment arm including ATO/ATRA and idarubicin with standard treatment based on ATRA plus chemotherapy (AIDA regimen).

Study design

Open label, randomized, prospective muliticenter, multinational phase III trial.

Intervention

Experimental intervention (Arm A): ATO/ATRA and idarubicin
Control intervention (Arm B): AIDA regimen for high-risk (ATRA plus chemotherapy)

Study burden and risks

Participation in this study will be associated with extra investigations compared to standard patient care. It is possible that the patient will

experience different adverse events in comparison to standard care. Furthermore, patients will be requested to participate in Quality of Life studies.

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

1.Informed consent
2.Women or men with a newly diagnosed APL by cytomorphology, confirmed by molecular analysis
3.Age >= 18 and <= 65 years
4.ECOG performance status 0-3
5.WBC at diagnosis > 10GPt/l
6.Serum total bilirubin <= 3.0 mg/dl (<=51 µmol/l)

7.Serum creatinine <= 3.0 mg/dl (<=260 µmol/l)
8.Women must fulfill at least one of the following criteria in order to be eligible for trial inclusion:
a.Post-menopausal (12 months of natural amenorrhea or 6 months amenorrhea with serum FSH > 40 U/ml)
b.Postoperative (i.e. 6 weeks) after bilateral ovariectomy with or without hysterectomy
c.Continuous and correct application of a contraception method with a Pearl Index of <1% (e.g. implants, depots, oral contraceptives, intrauterine device-IUD)
d.Sexual abstinence
e.Vasectomy of the sexual partner

Exclusion criteria

1.Patients who are not eligible for chemotherapy as per discretion of the treating physician
2.APL secondary to previous radio- or chemotherapy for non-APL disease
3.Other active malignancy at time of study entry (exception: basal-cell carcinoma)
4.Lack of diagnostic confirmation at genetic level
5.Significant arrhythmias, ECG abnormalities:
a.Congenital long QT syndrome
b.History or presence of significant ventricular or atrial tachyarrhythmia
c.Clinically significant resting bradycardia (<50 beats per minute)
d.QTc >500msec on screening ECG for both genders
e.Right bundle branch block plus left anterior hemiblock, bifascicular block
6.Other cardiac contraindications for intensive chemotherapy (L-VEF <50%)
7.Uncontrolled, life-threatening infections
8.Severe non controlled pulmonary or cardiac disease
9.Severe hepatic or renal dysfunction
10.HIV and/or active hepatitis C infection
11.Active multiple sclerosis (patients with inactive MS can be included)
12.Pregnant or breast-feeding patients
13.Allergy to trial medication or excipients in study medication
14.Substance abuse; medical, psychological or social conditions that may interfere with the patients participation in the study or evaluation of the study results
15.Use of other investigational drugs at the time of enrolment or within 30 days before study entry

Study design

Design

Study phase: 3

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-04-2018
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Trisenox
Generic name:	Arsenic trioxide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-06-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-04-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	22-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-11-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2015-001151-68-NL
CCMO	NL56512.042.16