A Randomized, open label, phase 2 study of the selective inhibitor of nuclear export (SINE) SELINEXOR (KPT-330) versus specified physician's choice in patients * 60 years old with relapsed/refractory acute myeloid leukemia (AML) who are ineligible for intensive chemotherapy and/or transplantation.

Published: 15-06-2014
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Primary Objective:To determine overall survival (OS) of Selinexor as compared to physician choice (PC) in patients * 60 years old with relapsed/refractory AML that requires treatment and are ineligible for intensive chemotherapy and/or...

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

Summary

ID

NL-OMON41919

Source
ToetsingOnline

Brief title
SOPRA-study

Condition

- Leukaemias

Synonym
acute myeloid leukemia, form of blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Karypharm Europe GmbH
Source(s) of monetary or material Support: Karyopharm Therapeutics;Inc

Intervention

Keyword: (SINE) Selinexor, AML, Inc., Karyopharm Therapeutics, Oncology

Outcome measures

Primary outcome

Primary efficacy endpoint: Overall survival.

Secondary outcome

* The proportion of patients whose OS is at least 3 months (OS3.0)

* The complete remission rate (CRR), including complete remission with full

hematologic recovery (CR), and median disease free survival (DFS) for patients

who achieve CR

* The modified CRR (mCRR), including CR or CRi (including CRp), and median DFS

for patients who achieve CR or CRi (including CRp)

* The overall response rate (ORR) and duration of overall response (DOR),

including CR, CRi, MLFS, and partial remission (PR)

* The disease control rate (DCR) defined as ORR + stable disease for * 4 weeks

(SD), and duration of DCR

* Quality of life and patient reported outcomes (FACT-Leukemia and EQ-5D-5L)

(QoL)

The safety and tolerability of selinexor and PC will be evaluated by means of

drug-related AE reports, physical examinations, and laboratory safety

evaluations.

Study description

Background summary

Selinexor (oral) has shown single-agent, durable, anti-cancer activity in patients with multiply relapsed or refractory hematologic and solid tumor malignancies in initial Phase 1 dose escalation studies.

Selinexor show potent antiproliferative effect and induced apoptosis, cell cycle arrest and myeloid differentiation in AML cell lines and patient blasts, including those from patients with NPM1 and FLT3-ITD mutations (Ranganathan 2012).

Oral Selinexor may represent a novel treatment for AML in this difficult-to-treat population.

Study objective

Primary Objective:
To determine overall survival (OS) of Selinexor as compared to physician choice (PC) in patients * 60 years old with relapsed/refractory AML that requires treatment and are ineligible for intensive chemotherapy and/or transplantation.

Secondary Objectives:
* To determine the proportion of patients whose OS is at least 3 months (OS3.0)
* To determine the complete remission rate (CRR), including complete remission with full hematologic recovery (CR), and median disease free survival (DFS) for patients who achieve CR
* To determine the modified CRR (mCRR), including CR or complete remission with incomplete hematologic recovery (CRi) (including complete remission with incomplete platelet recovery [CRp]), and median DFS for patients who achieve CR or CRi (including CRp)

* To determine the overall response rate (ORR) and duration of overall response (DOR), including CR, CRi, morphologic leukemia-free state (MLFS), and partial remission (PR)
* To determine the disease control rate (DCR) defined as ORR + stable disease for * 4 weeks (SD), and duration of DCR
* To assess the safety and tolerability of selinexor (KPT-330), as compared to physician's choice (PC)
* Quality of life and patient reported outcomes (FACT-Leukemia, EQ-5D-5L) (QoL)

Study design

This is a randomized, multicenter, open-label, Phase 2 study of the SINE Selinexor given orally versus specified investigator choices (one of three potential salvage therapies). Approximately 300 patients will be enrolled, with randomization of 2:1 Selinexor to PC arms.

One of the following three care regimens will be selected by the treating physician investigator (physician's choice - PC):
(1) BSC including blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea;
(2) BSC + low dose AraC, 20 mg bid by subcutaneous (sc) injection daily on Days 1-10/14 (20/28 doses) to be repeated at 28 to 42 day intervals; (3) BSC + hypomethylating agent: azacitidine 75 mg/m2 by sc injection daily on Days 1-7 or 1-5 and 8-9 (7 doses) to be repeated at *28 day intervals, or decitabine (20 mg/m2 IV over 1 hour daily on days 1-5 or days 1-10 to be repeated at * 28 day intervals).

Intervention

Study assessments:
sign informed consent, demographics, full ophthalmological and visual acuity examination, 12-lead ECG, concomitant medication assessments, chest radiograph, disease risk assessment according to ELN, physical examination, ECOG performance status, BSA, Vital signs, urine dipstick, serum chemistry, coagulation parameters, complete blood count, bone marrow aspirate (ore bipsy if aspirate is not adequate), blood draw for correlative studies using peripheral blasts, quality of life questionnaire (FACT-Leu), hematology (CBC with differential), selinexor dosing or physician's choice treatment, PK sampling, PD sampling, baseline symptoms, oxygen saturation, nutritional consultation, antineoplastic therapy and adverse event assessments, daily registration of body temperature during treatment until 30 days after termination of treatment..

Study burden and risks

Very common side effects (*20% or more than 1 out of 5 subjects):

* Nausea
* Anorexia - loss of appetite
* Fatigue
* Vomiting
* Weight loss
* Thrombocytopenia - low platelets
* Anemia - decrease in red blood cells

Less common (<20% or less 1 out of 5 subjects):
* Diarrhea
* Dysguesia - change in taste
* Dizziness
* Dehydration
* Constipation
* Dry mouth
* Changes in vision including blurred vision
* Decrease in neutrophils - a type of white blood cell that helps fight infections
* Decrease in white blood cells
* Low sodium

Rare side effects (*5% or less than 1 out of 20 subjects):
* worsening of pre-existing cataracts
* acute cerebellar syndrome * symptoms can include a sudden loss of coordination, balance, or slurred speech.
* Infection
* Sepsis * potentially life-threatening complication of an infection that has spread via the bloodstream.
* Pneumonia or inflammation of lung(s)

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

Patients age * 60 years with relapsed/refractory AML (defined using WHO criteria) of any type except for acute promyelocytic leukemia (APL; AML M3), who have poor prognosis (intermediate or adverse risk) cytogenetics, with relapsed or refractory AML, after at least one prior AML therapy (must have included an adequate trial of a hypomethylating agent with at least 2 cycles), who have never undergone, and who are not currently eligible for stem cell transplantation, and are currently deemed unfit for intensive chemotherapy.

Exclusion criteria

Patients with AML M3, known central nervous system (CNS) leukemia, who are in blast transformation of chronic myeloid leukemia (CML), or whose AML is classified as favorable according to the European LeukemiaNet (ELN) disease risk assessment will be excluded from this study.

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:	Recruitment stopped
Start date (anticipated):	08-03-2015
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Selinexor
Generic name:	XPO1

Ethics review

Approved WMO Date:	15-06-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	19-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	15-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2017
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	EUCTR2014-000920-26-NL
CCMO	NL48882.029.14

Study results

Date completed:	31-08-2017
Actual enrolment:	19