A Phase III randomized, double blind, placebo controlled, multicenter study of panobinostat for maintenance of response in patients with Hodgkinâ¤*s lymphoma who are at risk for relapse after high dose chemotherapy and autologous stem cell transplant

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Primary* To compare the disease free survival (DFS) in patients with HL after achieving a complete response following AHSCT with HDT who are treated with panobinostat versus those who receive placebo based on investigator*s review of radiological...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas Hodgkin's disease
Study type	Interventional

Summary

ID

NL-OMON36301

Source
ToetsingOnline

Brief title
Panobinostat study for Hodgkins lymphoma

Condition

- Lymphomas Hodgkin's disease

Synonym
Hodgkin's Lymphoma, malignant lymph-cell cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: double blind, Hodgkins lymphoma, placebo controlled, randomized

Outcome measures

Primary outcome

Primary efficacy endpoint:

* DFS

Secondary outcome

Secondary efficacy endpoints:

* OS

* RoR

Secondary safety endpoints:

* AEs as determined by Common Terminology Criteria for Adverse Events (CTCAE)

version 3 and SAEs

* Electrocardiogram (ECG) parameters

* Laboratory parameters

Secondary efficacy and safety endpoint:

* Pharmacokinetic parameter: Cmax Cmin

Study description

Background summary

To determine if panobinostat can aid to the reduction of relapse in classical Hodgkin Lymphoma patients

Study objective

Primary
* To compare the disease free survival (DFS) in patients with HL after achieving a complete response following AHSCT with HDT who are treated with panobinostat versus those who receive placebo based on investigator*s review of radiological images

Secondary
* To compare OS for the two arms
* To estimate and compare the RoR at 6, 12, and 24 months from randomization for the two arms
* To assess the safety and tolerability
* To characterize the safety and tolerability of panobinostat
* To explore the relationship of PK-PD (safety and efficacy) in patients with HL following AHSCT

Study design

Treatment phase/duration of treatment:
Starting cycle 1 day 1, all patients will be treated with study treatment (panobinostat 45 mg or placebo three times a week, every other week). The treatment duration is 52 weeks; one cycle consists of four consecutive weeks (28 days).
Patients will continue receiving study treatment until completion of study treatment (52 weeks) or until disease relapse, occurrence of intolerable toxicity, or withdrawal of consent; whichever occurs first.

Follow-up phase:
All patients enrolled to the study will be followed through the treatment period or until relapse and thereafter for progression and survival. Study results will be reported once adequate number of events (for DFS) have occurred.

Post-baseline radiological tumor assessments:
Radiological tumor assessments by CT/MRI for a patient will be performed for evaluation of relapse every 12 weeks from randomization for the first 24 months and every 16 weeks for the next 12 months. Thereafter, frequency of CT/MRI

scans will occur as per SOC. Patients will be followed for OS. This OS analysis will be presented at the end of the study and survival information will be updated five years after the last patient is enrolled in the study. Any clinical suspicion of disease recurrence at any time should be confirmed using a CT/MRI scan promptly rather than waiting for the next scheduled radiological assessment. The primary analysis of DFS will be based on a local radiological review of CT/MRI scan regardless of PET scan results.

Intervention

Not applicable

Study burden and risks

The patients physical situation is assessed by examinations and blood draws during (follow-up) visits and the progression/relapse of the disease is measured by CTor MRI scan lesions.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion
1. Patient age is *18 years
2. Patient has a history of histologically confirmed classical HL (i.e. Nodular sclerosing (NSHL), Mixed-cellularity (MCHL), Lymphocyte-rich (LRHL), Lymphocyte depleted (LDHL))
3. Patient has achieved a complete response by CT/MRI scan between 6 and 12 weeks from the day of their first autologous stem/bone marrow transfusion (AHSCT) following HDT. Where complete response is defined as:
Normalization of all nodes and lesions compared to pre-transplant scan performed prior to salvage therapy for relapse. Any residual abnormal masses on the post transplant CT/MRI must be metabolically inactive on a PET scan.
4. Patients must also have one of the following factors that places them at risk for relapse:
* Primary refractory disease (including relapse in * 3 months of completion of treatment)
* Multiple relapses (prior to transplant)
* First relapse >3 but <12 months from last dose of first-line treatment
* Stage III/IV disease (at relapse, prior to transplant)
* Hemoglobin <10.5 gm/dL (at relapse, prior to transplant)
5. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of * 2
6. Patient has the following laboratory values within 3 weeks of starting study drug (labs may be repeated, if needed, to obtain acceptable values before failure at screening is concluded)
* Absolute neutrophil count (ANC) * 1.5 x 109 /L
* Platelet count * 100 x 109 /L
* AST/SGOT and ALT/SGPT * 2.5 x ULN
* Serum total bilirubin * 1.5 ULN
* Serum creatinine * 1.5 x ULN
* Serum potassium, magnesium, sodium, total calcium (corrected for serum albumin) or ionized calcium within normal limits
Note: Potassium, magnesium, and/or sodium supplements (but not platelet or RBC transfusions) may be given to correct values that are < lower limit of normal (LLN). Post-correction values must not be deemed to be a clinically significant abnormality prior to patients being dosed.
7. Patient has the ability to swallow capsules
8. Sexually active patient (men and women of child bearing potential {WOCBP}) agrees to use double barrier method of contraception during the course of the study treatment period (52 weeks) and for 3 months after completing study treatment. WOCBP are defined as sexually mature women who have not undergone a hysterectomy or who have not been naturally postmenopausal for at least 12 consecutive months.
9. Patient has signed informed consent prior to any screening procedures

Exclusion criteria

Exclusion
1. Patient has been treated with allogeneic transplant
2. Patient has received any anti-lymphoma therapy after AHSCT including but not limited to:
* chemotherapy prior to start of study
* biologic immunotherapy including monoclonal antibodies or experimental therapy prior to start of study
* radiation therapy
3. Patient has not recovered from reversible toxicity due to any prior therapies (e.g. returned to baseline or Grade *1) except for hematological laboratory parameters
Note: Patient does not meet this criteria if the toxicity is stable and irreversible, and there is no evidence that panobinostat causes a similar toxicity
4. Patient who received prior treatment with DAC inhibitors including panobinostat
5. Patient who received an investigational agent of any kind within 28 days of randomization
6. Patient taking any anti-cancer therapy concomitantly
7. Patient with active central nervous system (CNS) disease or brain metastasis
8. Patient needs valproic acid within 5 days prior to first administration of panobinostat/ study treatment
9. Patients with evidence of another malignancy not in remission or history of such a malignancy within the last 3 years (except for treated basal or squamous cell carcinoma, or in situ cancer of the cervix).
10. Patient has undergone major surgery * 2 weeks prior to starting study drug or who have not recovered from side effects of such therapy to < grade 1 CTCAE or baseline
11. Patient has impaired cardiac function, including any one of the following:
* Left ventricular ejection fraction (LVEF) < the lower limit of institutional norm, as determined by echocardiogram (ECHO) or multiple uptake gated acquisition scan (MUGA)
* Obligate use of a permanent cardiac pacemaker
* Congenital long QT syndrome
* History or presence of ventricular tachy-arrhythmias
* Resting bradycardia defined as < 50 beats per minute
* QTcF > 480 msec on screening ECG
* Complete left bundle branch block, bifasicular block
* Any clinically significant ST segment and/or T-wave abnormalities
* Presence of unstable atrial fibrillation (ventricular response rate > 100 bpm). Patients with stable atrial fibrillation are allowed in the study provided they do not meet the other cardiac exclusion criteria.
* Myocardial infarction or unstable angina pectoris * 6 months prior to starting study drug
* Congestive heart failure (New York Heart Association class III-IV)
* Other clinically significant heart disease and vascular disease (e.g. uncontrolled hypertension)
12. Patient is taking medications with relative risk of prolonging the QT interval or inducing torsade de pointes, if such treatment cannot be discontinued or switched to a different medication prior to starting study drug
13. Patient has impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of panobinostat, such as:

* ulcerative disease
* uncontrolled nausea
* vomiting
* diarrhea CTCAE grade * 2
* malabsorption syndrome
* obstruction
* stomach and/or small bowel resection
14. Patient has any other concurrent severe and/or uncontrolled medical conditions that could cause unacceptable safety risks or compromise compliance with the protocol such as:
* uncontrolled diabetes
* active or uncontrolled infection
* chronic obstructive or chronic restrictive pulmonary disease including dyspnea at rest from any cause
* uncontrolled thyroid dysfunction
* recent, acute or active bleeding
15. Patient has a known history of human immunodeficiency virus (HIV) seropositivity or history of active/treated hepatitis B or C (a test for screening is not required)
16. Women who are pregnant or breast feeding

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2011
Enrollment:	58
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	panobinostat
Generic name:	LBH589

Ethics review

Approved WMO Date:	03-05-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2011
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	EUCTR2009-014846-26-NL
ClinicalTrials.gov	NCT01034163
CCMO	NL32040.029.10