A Phase 3, Randomized, Two-Arm, Open-Label, Multicenter, International Trial of Alisertib (MLN8237) or Investigator*s Choice (Selected Single Agent) in Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma

Published: 04-05-2012
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Primary:* To determine if alisertib improves overall response rate (ORR; complete response [CR] plus partial response [PR]) versus a selection of single agents in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)* To determine...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's T-cell
Study type	Interventional

Summary

ID

NL-OMON39884

Source
ToetsingOnline

Brief title
LUMIERE C14012- PTCL

Condition

- Lymphomas non-Hodgkin's T-cell

Synonym
Peripheral T-cel lymphoma

Research involving

Human

Sponsors and support

Primary sponsor: Millenium Pharmaceuticals
Source(s) of monetary or material Support: Millennium Pharmaceutical;Inc

Intervention

Keyword: Alisertib, Peripheral-T-Cell Lymphoma (PTCL), Phase 3

Outcome measures

Primary outcome

ORR: CR + PR based on independent review committee (IRC) assessment using the

IWG criteria.

PFS based on IRC assessment using the IWG criteria.

Secondary outcome

The key secondary endpoints are:

* CR rate

* Overall survival

Other secondary endpoints include:

* Adverse events (AEs), serious adverse events (SAEs), assessments of clinical

laboratory values and clinically important laboratory abnormalities, and vital

sign measurements

* Time to disease progression

* Duration of response

* Time to response

* Time to subsequent antineoplastic therapy

* Plasma concentration-time data to contribute to future population PK analysis

* Changes in reported symptoms and QOL assessment per FACT-Lym for functioning

and symptoms

Study description

Background summary

Aggressive peripheral T-cell lymphomas (PTCL) are rare malignancies and a biologically heterogeneous group of lymphomas. The majority of lymphoma treatments have been developed from studies dominated by the B cell lymphomas, resulting in approved indications for NHL which are not optimal for PTCL.
Initial treatments usually include a CHOP-based (cyclophosphamide, doxorubicin, vincristine, and prednisolone) regimen; however, even if a response is achieved, early relapse is common, and each subtype is associated with a varying prognosis. There is no consensus on standard treatment for this disease in the first-line setting and in the second-line setting outside of the US, and the available treatments are not optimal. Given the aggressive nature of this disease and with the poorest prognosis of all the NHL subtypes, PTCL patients represent an unmet medical need.
Alisertib is a selective small-molecule inhibitor of Aurora A kinase that is being developed for the treatment of advanced malignancies. Alisertib has demonstrated activity against a variety of nonclinical solid tumor and hematological malignancy models grown in vitro and in vivo. Multiple responses have been reported by objective criteria in patients with solid tumors, AML, and lymphomas who have received alisertib to date. In Study C14004, a phase 2, single-arm, multicenter study of alisertib in patients with aggressive forms of relapsed or refractory non-Hodgkin*s B- or T-cell lymphoma, 13 of the 48 enrolled patients achieved a response (ORR of 27%: 5 CR, 8 PR).

Study objective

Primary:
* To determine if alisertib improves overall response rate (ORR; complete response [CR] plus partial response [PR]) versus a selection of single agents in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)
* To determine if alisertib improves progression free survival (PFS) versus a selection of single agents in patients with relapsed or refractory PTCL

Key Secondary:
* To determine if alisertib improves CR rate
* To determine if alisertib improves overall survival (OS)

Other Secondary:
* To evaluate the safety and tolerability of alisertib in patients with relapsed or refractory PTCL
* To measure time to disease progression (TTP)
* To determine duration of response
* To measure time to response
* To measure time to subsequent antineoplastic therapy
* To collect pharmacokinetic (PK) data to contribute to population PK analyses
* To evaluate the impact of alisertib treatment versus control on the Quality of Life (QOL) through Functional Assessment of Cancer Therapy * Lymphoma (FACT-Lym) for functioning and symptoms

Study design

Phase 3, randomized, 2-arm, open-label, multicenter, international trial evaluating alisertib compared with single-agent treatment, as selected by the investigator from the offered options of pralatrexate or gemcitabine, in patients with relapsed or refractory PTCL.
Patients will be randomized (1:1) to study treatment, Arm A (alisertib) or Arm B (selected single-agent comparator: pralatrexate or gemcitabine).

Intervention

Patients will be randomized (1:1) to study treatment, Arm A (alisertib) or Arm B (selected single-agent comparator: pralatrexate or gemcitabine).

Study burden and risks

There is no consensus on standard treatment for PTCL and available treatments are not optimal. In previous studies where patients have been treated with alisertib, adverse events were generally reversible, dose-dependent, and consistent with the mechanism of alisertib. Alisertib shows encouraging early results. During this study, the patients are evaluated frequently while they are receiving treatment for their safety.

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. Male or females, age * 18 years
2. Patients with PTCL according to WHO criteria and have relapsed or are refractory to at least 1 prior systemic, cytotoxic therapy for PTCL. Patients must have received conventional therapy as a prior therapy (ie, experimental therapy may not be the only prior therapy). Cutaneous-only disease is not permitted. Patients must have documented evidence of progressive disease
3. Tumor biopsy available for central hematopathologic review
4. Measurable disease according to the IWG criteria (See Section 15.4). Patients must have at least 1 site of disease measurable in 2 dimensions by computed tomography (CT)
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0-2;Please see protocol for all inclusion criteria

Exclusion criteria

1. Known central nervous system (CNS) lymphoma
2. Systemic antineoplastic therapy, immunotherapy, investigational agent, or radiation therapy within 4 weeks of first dose of study treatment (6 weeks if nitrosoureas given) or concomitant use during study
3. Prior administration of an Aurora A kinase-targeted agent, including alisertib
4. Prior administration (whether in combination or as single-agent) of all 3 of the comparator drugs for the disease under study: pralatrexate, romidepsin, and gemcitabine;Please see

protocol for all exclusion criteria

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:	Recruitment stopped
Start date (anticipated):	04-07-2013
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alisertib
Generic name:	Alisertib
Product type:	Medicine
Brand name:	Folotyn
Generic name:	Pralatrexate
Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-05-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-08-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-03-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-11-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-11-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	16-05-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-09-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-02-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2011-003545-18-NL
ClinicalTrials.gov	NCT01482962
CCMO	NL39566.068.12