A phase II, multicenter, single-arm study of oral LDK378 in adult patients with ALK-activated non-small cell lung cancer previously treated with chemotherapy and crizotinib

Published: 19-11-2012
Last updated: 24-04-2024

The primary objective of the study is to demonstrate the antitumor activity of LDK378.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON41391

Source
ToetsingOnline

Brief title
LDK378 in NSCLC for patients previously treated with crizotinib

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
advanced non-small cell lung cancer, advanced NSCLC

Research involving
Human

Sponsors and support

Primary sponsor: Novartis

Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Keyword: ALK, LDK378, Non-small cell lung cancer

Outcome measures

Primary outcome

Tumor response per RECIST v1.1 as assessed by the investigators.

Secondary outcome

- Duration of response (DOR)

- Disease control rate (DCR)

- Time to Response (TTR)

- Overall response rate (ORR) by assessment by a Blinded Independent Review

Committee (BIRC)

Study description

Background summary

Lung cancer has been the most common cancer in the world. Non-small cell lung cancer (NSCLC) accounts for more than 85% of all lung cancer cases. The prognosis continues to be poor despite chemotherapy treatment, with a 5-year overall survival rate of only 15%.
During the last few years, improved knowledge of NSCLC biology led to the identification of molecular events crucial for malignant transformation and cancer cell survival.
Multiple large randomized clinical trials have demonstrated that patients harboring activating EGFR mutations benefit more from EGFR TKIs than from standard chemotherapy. The success of EGFR TKIs highlights the importance of identifying specific NSCLC molecular drivers to appropriately direct targeted agents to specific patient populations.
The discovery of anaplastic lymphoma kinase (ALK) rearrangement in NSCLC in 2007 represents another important milestone in the era of molecular targeted therapy in NSCLC.
The frequency of EML4-ALK rearrangement in patients with NSCLC is relatively

low; it is present in approximately 2-8% of tumors tested. However, considering the high incidence of lung cancer, this small percentage translates into about 10,000 patients in the United States alone.
Crizotinib, an orally available small-molecule inhibitor of ALK and MET tyrosine kinases, has been rapidly and successfully developed in patients with advanced NSCLC who have EML4-ALK rearrangements
While crizotinib has impressive activity in patients with ALK rearranged NSCLC, these cancers invariably progress, typically within 1 year, because of the development of resistance to crizotinib. For these patients there is no alternative ALK-targeted therapy. Therefore, the development of ALK TKIs with clinical activity against ALK-positive NSCLC resistant to crizotinib is crucial.

Study objective

The primary objective of the study is to demonstrate the antitumor activity of LDK378.

Study design

This is a single-arm, open-label, multicenter, phase II study.

Intervention

LDK378 will be administered orally once daily at a dose of 750 mg on a continuous dosing schedule.

Study burden and risks

* Study duration in principle until disease progression. Thereafter follow-up for survival.
* The screening phase with extensive assessments. Bi-weekly visits during the first cycle and a monthly visit thereafter.
* PK blood sampling on day 1 of the first 6 cycles and extra PK blood sampling until 6hours post dose and the next day (24hrs post dose) on day one of cycle 1 and 2 for a limited number of patient at selected sites (in the Netherlands this will be only at the UMCG).
* Physical examination at every visit.
* There will be extra blood drawn during the study visits. Approximately 3-4ml per visit and an additional 10ml for extra PK samples.
* Pregnancy test at screening.
* ECG at every visit and additional ECGs for patients were extra PK samples are taken.
* Optional tumor biopsy at the screening and at the end of treatment.
* Optional donation of left-over tumor tissue for future testing.

Contacts

Public
Novartis

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Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Histologically or cytologically confirmed diagnosis of locally advanced or metastatic NSCLC that carries an ALK rearrangement, as per the FDA-approved FISH assay (Abbott Molecular Inc.).
* Patients must have NSCLC that has progressed during therapy with crizotinib or within 30 days of the last dose
* Patients must have received 1-3 lines of cytotoxic chemotherapy (of which 1 must have been a platinum doublet) to treat their locally advanced or metastatic NSCLC
* Patients must have archival tissue sample available, collected either at the time of diagnosis of NSCLC or any time since.
*Patients must have recovered from all toxicities related to prior anticancer therapies to grade * 2, except for patients with grade 2 nausea/vomiting and/or grade 2 diarrhea despite optimal supportive therapy who will not be allowed to participate in the study.

Exclusion criteria

* Patients with known hypersensitivity to any of the excipients of LDK378.
* Patients with symptomatic central nervous system (CNS) metastases who are neurologically unstable or have required increasing doses of steroids within the 2 weeks prior to study entry to manage CNS symptoms.
* History of carcinomatous meningitis.
* Presence or history of a malignant disease other than NSCLC that has been diagnosed and/or required therapy within the past 3 years.
* Clinically significant, uncontrolled heart disease

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-01-2013
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Zykadia
Generic name:	ceritinib

Ethics review

Approved WMO Date:	19-11-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-04-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2015
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	EUCTR2012-003432-24-NL
ClinicalTrials.gov	NCT01685060
CCMO	NL42258.042.12