A Phase I, open-label, dose escalation study of LDK378 in pediatric patients with malignancies that have a genetic alteration in anaplastic lymphoma kinase (ALK)

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Primary objective: Estimate the MTD and/or RDE of LDK378 as a single agent when administered orally to pediatric patients with ALK-activated tumors in the fasted and in fed stateSecondary objectives: Objective 1: Characterize the safety and...

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

Summary

ID

NL-OMON46950

Source
ToetsingOnline

Brief title
CLDK378X2103

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
malignancies with ALK-aberrations, pediatric cancer

Health condition

Alle maliginiteiten met een ALK mutatie.

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: ALK gene aberrations, LDK378, pediatric, Phase I

Outcome measures

Primary outcome

Primary endpoint: Incidence rate of Dose Limiting Toxicities (DLT) during the first cycle of LDK378 treatment.

Secondary outcome

Secondary endpoints:

Endpoint 1: Adverse events and serious adverse events, changes in laboratory values, assessments of physical examinations, vital signs and electrocardiograms.

Endpoint 2: Plasma concentration time profiles, PK parameters, including but not limited to AUClast, AUCtau, Cmin, Cmax, Tmax, Racc, and T1/2,acc

Endpoint 3: Overall response rate (ORR) and duration of response (DOR), progression-free survival (PFS) as per RECIST 1.1 in patients with neuroblastoma and other solid tumors, and by International Working Group (IWG) criteria in patients with lymphoma. MIBG response in patients with neuroblastoma. Resolution of bone marrow disease in patients with neuroblastoma.

Study description

Background summary

LDK378 is a novel inhibitor of ALK that is active in a broad range of ALKactivated tumor models, including models driven by mutated versions of ALK known to be resistant to crizotinib, and by ALK gene amplification. The primary purpose of this study is to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) in pediatric patients in the fasted and in fed state, and to delineate a clinical dose to be used in any future pediatric
studies. This study will also assess the safety, tolerability, PK and preliminary evidence of antitumor activity of LDK378 in pediatric patients with neuroblastoma, and other ALK-activated tumors.

Study objective

Primary objective: Estimate the MTD and/or RDE of LDK378 as a single agent when administered orally to pediatric patients with ALK-activated tumors in the fasted and in fed state

Secondary objectives:
Objective 1: Characterize the safety and tolerability of LDK378 in pediatric patients in the fasted and in fed state

Objective 2: Characterize single and multiple-dose PK of LDK378 in pediatric patients in the fasted and in fed state

Objective 3: Assess the anti-tumor activity of LDK378 in the fasted and in fed state

Study design

This is a two-part, phase 1 study, with a dose escalation part followed by an expansion part. The expansion part will start after the MTD/RDE has been determined. The expansion part will include 2 groups of patients, one restricted to patients with ALK-activated neuroblastoma in the fasted and in fed state and the second including patients with all other ALK-activated tumors. Enrollment will proceed in parallel. LDK378 will be administered orally, once daily, continuously.

Intervention

Children will be treated with oral LDK378 long as they will benefit from it.

Response assessment every 21 days.

Study burden and risks

Risk:
Side effects of the study medication (see also the dose-limiting toxicities described on page 35, Table 6-2), drawing blood samples and tissue biopsies. Het collection of blood can cause a bruise, bleeding at the site or blood clothing. These usually disappear naturally.

Burden:
-study visits 2 times per 21 days for 2 years after proceeding though the screening.
-blood draws for lab tests every visit
-other assesments such as tissue biospies, ECGs and radiology tests.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Diagnosed with a locally advanced or metastatic malignancy that has progressed despite standard therapy, or for which no effective standard therapy exists ;- Age * 12 months and <18 years ;- The tumor must carry a genetic alteration of ALK ;- Patients must have evaluable or measurable disease;Other protocol-defined inclusion criteria may apply

Exclusion criteria

- Symptomatic central nervous system (CNS) metastases who are neurologically unstable or require increasing doses of steroids or local CNS-directed therapy (such as radiotherapy, surgery or intrathecal chemotherapy) to control their CNS disease ;- Clinically significant, uncontrolled heart disease ;- Inadequate end organ function as defined by specified laboratory values;- History of known of interstitial lung disease or interstitial pneumonitis, including
clinically significant radiation pneumonitis (i.e., affecting activities of daily living or requiring therapeutic intervention).;-Radiotherapy to lungs * 4 weeks prior to starting the study treatment or
patients who have not recovered from radiotherapy related toxicities. For
all other anatomic sites, radiotherapy * 2 weeks prior to starting the study treatment.;- Use of medications that are known to be strong inhibitors or inducers of CYP3A4/5 that cannot be discontinued at least 1 week prior to start of treatment with LDK378 and for the duration of the study ;- Use of medications that are mainly metabolized by CYP3A4/5 or CYP2C9 that cannot be discontinued at least 1 week prior to start of treatment with LDK378 and for the duration of the study.;- Patient has a history of pancreatitis or history of increased amylase or lipase that was due to pancreatic disease.;Other protocol-defined exclusion criteria may apply

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):	12-09-2013
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ceritinib
Generic name:	zykadia
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-05-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-08-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	14-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2015

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-08-2018
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2012-002074-31-NL
CCMO	NL43465.078.13