A Phase 1b/Adaptive Phase 2 Study of Docetaxel With or Without MLN1117 in Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer

Published: 12-06-2015
Last updated: 16-04-2024

Phase 2: To evaluate progression-free survival (PFS) as the primary efficacy measure of MLN1117 plus docetaxel versus docetaxel alone in patients with advanced NSCLC

Ethical review	Approved WMO
Status	Will not start
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON42595

Source
ToetsingOnline

Brief title
MLN1117 With or Without Docetaxel

Condition

- Metastases

Synonym
Locally Advanced or Metastatic, lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: metastatic, Non-small cell lung cancer, Oncology

Outcome measures

Primary outcome

Phase 2

- Progress-Free Survival (PFS) collected during the posttreatment follow-up

period of up to 6 months after the last dose of study drug

Secondary outcome

Endpoints for phase 2 at any time during phase 2 of the study

- Safety:

o Vital signs

o Physical examination findings

o 12-lead ECG

o Clinical laboratory test results

o AEs and SAEs

- Response rate (complete response [CR] + partial response [PR]), disease

control rate (CR + PR + stable disease [SD]), duration of response (DOR), and

TTP

- Overall Survival

- MLN1117 plasma concentrations when administered 1 day after

docetaxel

Study description

Background summary

MLN1117 is an orally available, potent, and selective small molecule inhibitor of the class I phosphoinositide 3-kinase (PI3K) alpha isoform (PI3K). It is being developed for the treatment of malignancies in which the PI3K pathway is believed to contribute significantly to the pathologic process and response to the standard therapies.
MLN1117 is also being developed in combination with MLN0128 (a novel, highly selective, orally bioavailable adenosine 5* triphosphate (ATP)-competitive inhibitor of the
serine/threonine kinase referred to as the metabolic target of rapamycin [mTORr]) as a
treatment for advanced nonhematologic malignancies.

Study objective

Phase 2: To evaluate progression-free survival (PFS) as the primary efficacy measure of MLN1117 plus docetaxel versus docetaxel alone in patients with advanced NSCLC

Study design

An open-label, phase 1b/adaptive phase 2 study of MLN1117 in combination with docetaxel versus docetaxel alone in adult patients with NSCLC. This study consists of a Phase 1b dose escalation phase, and an adaptive, randomized Phase 2 expansion phase.

Intervention

In Phase 2, the expansion phase of the study, up to 140 patients may be treated with the dose of MLN1117 that in combination with docetaxel is identified in Phase 1b as the RP2D (Arm A) or docetaxel alone (Arm B).
- Arm A: docetaxel 36 mg/m2 IV on Days 1 and 8 of a 21-day cycle plus MLN1117 tablets, at the dose determined in Phase 1b, on Days 2, 3, 4, 9, 10, 11, 16, 17, and 18
of a 21-day cycle
- Arm B: docetaxel 75mg/m2 IV once every 3 weeks (per approved prescribing information) with dosing on Day 1 of each 21-day cycle

Study burden and risks

MLN1117 is a selective inhibitor of PI3K* that might provide a better tolerability profile than pan-PI3K inhibitors.

Possible risks for MLN1117 are: Grade 1 through 3 nonserious hyperglycemia events, Grade 1 through 3 increases in ALT and/or AST, Nausea and vomiting. Patients treated with docetaxel commonly experience bone marrow suppression, gastrointestinal events, fatigue, and hair loss.
Taken together, the safety data of MLN1117 and docetaxel as single agents indicate that the combination of these 2 agents may lead to increased gastrointestinal toxicities that should be generally reversible. The combination of MLN1117 and docetaxel may
lead to exacerbation of non-overlapping toxicities and the occurrence of new toxicities that have not been identified with the single agents.*

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*Has a histologically and/or cytologically confirmed diagnosis of NSCLC (squamous or nonsquamous).
*For Phase 2, has a diagnosis of mixed squamous and nonsquamous (or adenosquamous) NSLC.
*Has locally advanced or metastatic disease (Stage IIIb or Stage IV) with radiographically or clinically evaluable lesions.
*Has experienced failure of at least 1 prior chemotherapy regimen.
*For Phase 2, has received 1 prior platinum-based chemotherapy regimen (excluding a docetaxel-containing regimen) for advanced or metastatic (Stage IIIb or Stage IV) disease followed by documented progressive disease.
*For Phase 1b, has experienced failure of multiple lines of prior chemotherapy.
*For Phase 2, has archived or fresh tumor biopsy samples obtained during screening sufficient for genotyping.
*Has adequate organ function, before the first dose of study drug.
*Has Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1.
*Female participants who are postmenopausal for at least 1 year before the screening visit or are surgically sterile, or are of childbearing potential, agree to practice 1 highly effective method and 1 additional effective (barrier) method of contraception, at the same time, from the time of signing the informed consent through 30 days (or longer, as mandated by local labeling [eg, USPI, SmPC, etc]) after the last dose of study drug, or agree to practice true abstinence.
*Male participants agree to practice highly effective barrier contraception during the entire study treatment period and through 120 days after the last dose of MLN1117 and, for docetaxel, for as long as is mandated by local labeling (eg, USPI, SmPC, etc), or agree to practice true abstinence.
*Has suitable venous access for the study-required blood sampling.
*Has recovered (ie, <<= Grade 1 toxicity or eligibility per this protocol is met) from the reversible effects of prior anticancer therapy.

Exclusion criteria

*Previous treatment with a PI3K or AKT inhibitor.
*Prior cancer therapy or other investigational therapy within 2 weeks before the first administration of study drug or failed to recover from the reversible effects of prior anticancer therapies. For prior therapies with a half-life longer than 3 days, the interval must be at least 28 days before the first administration of study drug, and the patient must have documented progressive disease.
*Has poorly controlled diabetes mellitus defined as HbA1c > 6.5%.
*Has taken strong inhibitors or strong inducers of CYP3A4 within 14 days before the first dose of study drug.

*Has taken histamine-H2 receptor antagonists and/or neutralizing antacids within 24 hours before the first administration of study drug.
*Has taken proton pump inhibitors within 7 days before the first administration of study drug.
*Has any clinically significant co-morbidities.
*Has acute myocardial infarction within 6 months before starting study drug, current or history of New York Heart Association Class III or IV heart failure, Evidence of current uncontrolled cardiovascular conditions including cardiac arrhythmias, angina, pulmonary hypertension, or ECG evidence of acute ischemia or active conduction system abnormalities, Fridericia's corrected QT interval > 475 milliseconds (msec) (males) or > 450 msec (females) on a 12-lead ECG during the Screening period, or abnormalities on 12-lead ECG including, but not limited to, changes in rhythm and intervals that in the opinion of the investigator are considered to be clinically significant.
*Has known, previously diagnosed human immunodeficiency virus infection or active chronic hepatitis B or C.
*Has brain metastasis, except for those patients who have completed definitive therapy, are not on steroids, have a stable neurologic status for at least 2 weeks after completion of the definitive therapy and steroids, and do not have neurologic dysfunction that would confound the evaluation of neurologic and other adverse events.
*Has active secondary malignancy that requires treatment.
*Has any serious medical or psychiatric illness, including drug or alcohol abuse.
*Male participants who intend to donate sperm during the course of this study or 120 days after receiving their last dose of study drug.
*Female participants who are lactating and breastfeeding or have a positive serum pregnancy test during the Screening period or a positive urine pregnancy test on Day 1 before administration of the first dose of study drug

Study design

Design

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

Recruitment

NL
Recruitment status: Will not start

Enrollment:	11
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	L01CD02
Generic name:	Docetaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	TAK-117 (MLN1117)
Generic name:	NA

Ethics review

Approved WMO Date:	12-06-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-10-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-11-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-11-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-004281-25-NL
ClinicalTrials.gov	NCT02393209
CCMO	NL52725.056.15