A Randomized Phase 3 Study of Ganetespib in Combination with Docetaxel versus Docetaxel Alone in Patients with Advanced Non-Small-Cell Lung Adenocarcinoma

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Primary Objectives* Compare OS in NSCLC patients with adenocarcinoma histology treated with ganetespib in combination with docetaxel versus docetaxel aloneSecondary Objectives* Compare progression-free survival (PFS) between the 2 treatment arms*...

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

Summary

ID

NL-OMON41451

Source
ToetsingOnline

Brief title
9090-14 (Galaxy-2)

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
ADVANCED NON-SMALL-CELL LUNG ADENOCARCINOMA; Lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Synta Pharmaceuticals Corporation
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: □ Adenocarcinoma, □ HSP90 inhibitor, □ NSCLC

Outcome measures

Primary outcome

Overall Survival (OS)

Secondary outcome

progression-free survival (PFS);

objective response rate (ORR);

disease control rate (DCR);

duration of response (DOR)

Study description

Background summary

Please refer to the study protocol section 5.1. "Scientific Background"

Study objective

Primary Objectives
* Compare OS in NSCLC patients with adenocarcinoma histology treated with ganetespib in combination with docetaxel versus docetaxel alone

Secondary Objectives
* Compare progression-free survival (PFS) between the 2 treatment arms
* Compare OS between the 2 treatment arms in patients with elevated screening serum lactate dehydrogenase (eLDH)

Other Secondary Objectives
* Compare objective response rate (ORR). disease control rate (DCR), and

duration of response (DOR) between the 2 treatment arms
* Compare PFS, ORR, and DCR between the 2 treatment arms in patients with screening serum eLDH, and patients with elevated screening serum LDH5 (eLDH5)
* Compare OS between the 2 treatment arms in patients with screening serum eLDH5
* Compare the emergence of metastatic lesions between the 2 treatment arms
* Evaluate the safety of study treatments in this patient population
* Compare patient quality of life as measured by the European Quality Of Life - Five Dimensions - Three Levels (EQ-5D-3L) test between the 2 treatment arms
* Compare symptom improvement as measured by the Functional Assessment of Cancer Therapy * Lung (FACT-L) version 4 test between the 2 treatment arms
* Assess the correlation between biomarkers, including KRAS status, and clinical outcome

Study design

This is an open-label, multicenter, randomized Phase 3 study of patients with advanced (Stage IIIB/IV) NSCLC of adenocarcinoma histology. Eligible patients must have failed only 1 prior systemic therapy for advanced NSCLC and have measurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST).

Patients will be randomized in a 1:1 ratio to receive either ganetespib in combination with docetaxel or docetaxel alone. The study will compare the efficacy and tolerability of ganetespib in combination with docetaxel versus docetaxel alone.

The study will enroll approximately 850 patients diagnosed *6 months prior to study entry with advanced NSCLC and adenocarcinoma histology in order to obtain approximately 700 patients whose tumors are negative for both EGFR mutations and ALK translocations. Patients will be randomized into one of two treatment arms:
* Arm A (control arm): Docetaxel 75 mg/m2
* Arm B (combination arm): Ganetespib 150 mg/m2 in combination with docetaxel 75 mg/m2.

The study will be divided into the following phases:
* Screening Phase.
* Randomization Phase.
* Treatment and Ganetespib Maintenance Phase.
* Follow-Up Phase.

Intervention

* Arm A (control arm): Docetaxel 75 mg/m2 will be administered on Day 1 of a

3-week treatment cycle by 1-hour intravenous infusion

* Arm B (combination arm): Ganetespib 150 mg/m2 in combination with docetaxel 75 mg/m2. On Day 1 of each 3-week treatment cycle, ganetespib and docetaxel will be administered as separate 1-hour intravenous infusions. Administration of ganetespib will precede the administration of docetaxel. There will be a 1-hour *rest* period following the end of the ganetespib infusion prior to docetaxel
infusion. Ganetespib 150 mg/m2 will be administered again on Day 15 of each cycle

Study burden and risks

Risks which are associated with the study procedures (e.g., drug administration via infusion, tumour biopsy, MRI, CT scan, etc) are described in detail in the Patient Information sheet and informed consent form (please refer to section"Risks of study procedures").
There might be drug-related side effects which are described in the the section "What are the risks of being in this study?" of the Patient Information sheet and informed consent form.
Ganetespib has potent single-agent activity in NSCLC lines in vitro and in vivo. It has been further demonstrated that ganetespib synergistically enhances the antitumor activity of taxanes in preclinical NSCLC models. Combinations of ganetespib with either docetaxel or paclitaxel were more effective than single agent treatments at inducing cell death.
As of today Ganetespib is being studied in 25 phase I and Phase II clinical trials, both Synta-sponsored and Investigator-sponsored. Gantespib has been administered to more than 600 patients. Clinical results shows good tolerability and efficacy of ganetespib.
An encouraging overall survival signal and a favorable safety profile have been demonstrated in an interim analysis from the ongoing Phase 2B trial designed to evaluate the efficacy and safety of ganetespib in combination with standard-of-care docetaxel versus docetaxel alone as second-line treatment for patients with advanced NSCLC.
Based on the results to date, the sponsor believes that ganetespib in combination with standard-of-care docetaxel as second-line treatment for patients with advanced NSCLC will have an improved survival compared to docetaxel (standard of care treatment) given alone.

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

A patient is eligible for the study if all of the following criteria are met:
1. Age 18 years or older
2. Pathologically confirmed diagnosis of NSCLC, with predominantly adenocarcinoma histology. Tumors must be negative for both EGFR mutations and ALK translocations.
3. Stage IIIB/IV NSCLC
4. Only one prior systemic therapy for Stage IIIB/IV disease defined as a platinum-based combination chemotherapy
5. Diagnosis of advanced NSCLC *6 months prior to signing of informed consent document
6. Documented disease progression during or following first-line therapy for advanced disease
7. Measurable disease
8. Available archived tumor tissue block with sufficient tumor tissue for biomarker testing; alternatively unstained slides with sufficient tumor tissue may be substituted. If archived tissue is not available, a fresh biopsy will be obtained during the screening period.
9. ECOG PS 0 or 1
10. Adequate hematologic function defined as:
* Absolute neutrophil count (ANC) *1.5 × 10(9)/L
* Hemoglobin *9 g/dL

11. Platelets *100 × 10(9)/L Adequate hepatic function defined as:
* Albumin *3 g/dL
* Serum total bilirubin *1.5 x ULN
* Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)
*1.5 × ULN without liver metastases; *5 × ULN if documented liver metastases
12. Adequate renal function defined as:
* Serum creatinine *1.5 x ULN or calculated creatinine clearance (cCrCl) per Cockcroft-Gault formula * 50mL/min
13. Negative serum human chorionic gonadotropin pregnancy test at study entry for patients of childbearing potential. Patients of reproductive potential must agree to use adequate contraception for the duration of study treatment and for 30 days after the last dose of ganetespib, and for 3 months (women) and 6 months (men) after the last dose of docetaxel since docetaxel can have genotoxic effects and may alter male fertility.
14. Ability to understand, and willingness to sign, a written informed consent document and to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures.

Exclusion criteria

1. Predominantly squamous, adenosquamous histology, or unclear histologic type
2. Prior maintenance therapy with an investigational anticancer agent
3. Prior treatment with tyrosine kinase inhibitors (TKIs) for lung cancer.
4. Patients with tumors known to harbor molecular alterations for which a targeted therapy is approved.
NOTE: Patients whose tumors have not been tested for molecular alterations for which a targeted therapy is approved are not eligible.
5. Presence or suspicion of central nervous system (CNS) metastases and/or leptomeningeal carcinomatosis as determined by magnetic resonance imaging/computed tomography (MRI/CT) scan performed at screening.
NOTE: Patients who have stable CNS metastases for at least 2 weeks following completion of radiotherapy are eligible
6. Active malignancies other than NSCLC within the last 5 years except for adequately treated in situ carcinoma of the cervix uteri, or basal or squamous cell carcinoma of the skin
7. Significant weight loss defined as *10% body weight within the 4 weeks prior to randomization
8. History of pulmonary hemorrhage or hemoptysis National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) *Grade 2 within 4 months of randomization
9. Peripheral neuropathy NCI CTCAE *Grade 2 at baseline
10. Patients with only 1 measurable lesion that was exposed to prior radiotherapy; the exception is lesions with documented disease progression with new tissue growth of at least 1 cm in longest diameter compared to nadir scan.
NOTE: Patients must have completed treatment and recovered from all acute treatment-related toxicities prior to administration of first dose of study drug
11. Known serious cardiac illness or medical conditions, including but not limited to:
i. Clinically unstable cardiac disease, including unstable atrial fibrillation, symptomatic

bradycardia, unstable congestive heart failure, active myocardial ischemia, or indwelling temporary pacemaker
ii. Ventricular tachycardia or a supraventricular tachycardia that requires treatment with a Class Ia antiarrhythmic drug (eg, quinidine, procainamide, disopyramide) or Class III antiarrhythmic drug (eg, sotalol, amiodarone, dofetilide). Use of other antiarrhythmic drugs is permitted.
iii. Use of medications that have been linked to the occurrence of torsades de pointes
iv. Second- or third-degree atrioventricular (AV) block unless treated with a permanent pacemaker
v. Complete left bundle branch block (LBBB)
vi. History of long QT Syndrome or a family member with this condition
vii. QTc >470 ms (average of triplicate ECG recordings). A consistent method of QTc calculation must be used for each patient's QTc measurements. QTcF (Fridericia's formula) is preferred.
viii. Serum potassium, magnesium, or calcium levels outside the laboratory's reference range
12. Uncontrolled intercurrent illness including, but not limited to, patients receiving combination antiretroviral therapy or patients with severe or systemic infection, or psychiatric illness/social situations that would limit compliance with study requirements.
13. Other severe acute/chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, and in the judgment of the investigator would make the patient inappropriate for entry into this study.
NOTE: Patients with a history, or at a risk, of pulmonary embolism are eligible with appropriate use of anti-coagulant therapy.
14. Women who are breastfeeding

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):	01-08-2014
Enrollment:	34
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Docetaxel
Generic name:	Docetaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ganetespib
Generic name:	Ganetespib

Ethics review

Approved WMO Date:	22-08-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-01-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-03-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	03-04-2014
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:	25-06-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-09-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-10-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-03-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-10-2015
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	EUCTR2012-004349-34-NL
ClinicalTrials.gov	NCT01798485
CCMO	NL45446.068.13