A phase II, multicenter, randomized, two-arm study of capmatinib (INC280, an oral MET inhibitor) and spartalizumab (PDR001, a PD-1 inhibitor) combination therapy versus docetaxel in pretreated adult patient with EGFR wild-type, ALK rearrangement negative locally advanced/metastatic non-small cell lung cancer.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON48017

Source
ToetsingOnline

Brief title
CINC280D2201

Condition

- Miscellaneous and site unspecified neoplasms benign
- Respiratory tract neoplasms

Synonym
non-small cell lung cancer; lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: capmatinib, docetaxel, NSCLC, spartalizumab

Outcome measures

Primary outcome

In the run-in part safety and tolerability data will be assessed when all patients in this phase have at least 24 weeks of follow-up as well as preliminary efficacy.

Secondary outcome

In the randomized part, the primary analysis will be performed when approximately 60 overall survival events have been observed. Overall Survival (OS) is defined as the time from the date of randomization/start of treatment to date of death due to any cause. A cut-off date will be established for analysis of OS. All deaths occurring on or before the cut-off date in the Full Analysis Set (FAS) will be used in the OS analysis. If a patient is not known to have died at the time of analysis cut-off, OS will be censored at the date of last contact. The analysis of OS will be based on full analysis set which

includes who received at least one dose of any component of study treatment and all randomized subjects. The estimated hazard ratio (HR) between capmatinib and spartalizumab combination and docetaxel and exact 80% confidence interval will be assessed. The expected median OS for docetaxel as second-line chemotherapy is ~8 months (Herbst et al 2016, Rittmeyer et al 2017). A 33.3% reduction in hazard rate for overall survival in capmatinib plus spartalizumab arm compared to docetaxel arm will correspond to an increase in median OS by 4 months under the exponential assumption. Considering a 2:1 randomization, with approximately 60 OS events, the probability

of observing clinically relevant activity is 66% when the true HR is 0.60 and the probability of observing clinically relevant activity is 24% when the true HR is 0.80. The secondary efficacy endpoints, objective response rate (ORR), disease control rate (DCR), progression free survival (PFS), time to response (TTR), duration of response (DOR) and disease control rate (DCR) based on the investigator assessed as per RECIST 1.1 will be analyzed.ORR and DCR will be summarized with accompanying 95% confidence interval (CI). PFS, TTR, DOR and the Kaplan-Meier curves, medians and 95% confidence intervals of the medians will be presented.

Study description

Background summary

Capmatinib is in a tablet that is taken by mouth. It is a so-called targeted medicine. This means that it is aimed at a certain process that does not work well in the cancer cells in your body. It is possible that your lung cancer is caused thereby.

Spartalizumab is a so-called monoclonal antibody. That is a protein that attaches itself to a certain body protein, called PD-1. As a result, spartalizumab can increase the efficacy of certain cells of the body's immune system. This allows the immune system of the body to better fight the tumor cells. This can then delay tumor growth.
The combination of capmatinib and spartalizumab is currently being tested in the form of a liver cancer. There are also reasons to believe that this combination has a beneficial effect in patients with NSCLC.
Capmatinib and spartalizumab are not yet authorized ("registered") by the Dutch government as a medicine. Doctors are therefore not allowed to prescribe the drugs to patients with NSCLC or other diseases. Registration with patients is required for registration.
As mentioned, docetaxel is the standard treatment for the type of lung cancer you have. Docetaxel is a form of chemotherapy and is a cell-killing substance.
In the current study we want to compare the efficacy and safety of the combination of capmatinib and spartalizumab with the effects of docetaxel. Docetaxel has been registered for the treatment of advanced or metastatic NSCLC. Administration of docetaxel is done in the way it is registered. Capmatinib and spartalizumab are made by Novartis and docetaxel by another company.
The research consists of two parts. You participate in one of both parts:
Part 1: Part 1 is performed to assess the safe and tolerated doses of capmatinib and spartalizumab. Approximately 15 test subjects participate in part 1.
Part 2: In part 2 the efficacy, safety and tolerability of the combination of capmatinib and spartalizumab are compared with those of docetaxel. Approximately 90 test subjects participate in part 2.

Study objective

The aim of this prospective, multicentre randomized phase II study is to evaluate the safety and efficacy of the combination of capmatinib and spartalizumab in subjects with EGFR weight (for exon 19 deletions and exon 21 L858R substitution mutations), ALK-negative rearrangement, advanced / metastatic (stage IIIB (not susceptible to definitive chemo-radiotherapy) or IV) NSCLC, regardless
MET and PD-L1 status The study will enroll test subjects with advanced / metastatic NSCLC who are EGFR-wt, ALK-negative, after failure of previous platinum doublet and calibration point inhibitor administered for the treatment of the advanced stage disease. Topics must be
docetaxel naive. A run-in part is performed to determine the safety and tolerability and preliminary efficacy of the combination of capmatinib and spartalizumab. Randomized part will be performed to assess the overall survival (OS) of the combination of capmatinib and spartalizumab compared with docetaxel

Study design

This is a two-part prospectively designed, multicenter, open-label, randomized phase II study to evaluate the safety and the efficacy of capmatinib in combination with spartalizumab in adult subjects with EGFR wild type and ALK rearrangement negative advanced stage IIIB or IV NSCLC after failure of platinum doublet chemotherapy and checkpoint inhibitor treatment. Part 1: run-in phase: will confirm the safety and tolerability and assess the efficacy of the combination of capmatinib and spartalizumab. Part 2: randomized phase: will evaluate the efficacy and safety of the combination of capmatinib and spartalizumab compared to docetaxel

Intervention

Treatment with capmatinib and spartalizumab combination or docetaxel.

Study burden and risks

Subjects in this study have advanced non-small cell lung cancer and have progressed after one or two lines of prior approved chemotherapy, radiotherapy and/or immunotherapy. Given the clinical and molecular characteristics of their disease they have limited therapeutic options and
the established standard, single agent chemotherapy regimens approved for this setting are of limited benefit. Synergistic antitumor effect has been shown preclinically with capmatinib in combination with checkpoint inhibitors in non-MET driven tumor models. The safety profile of capmatinib and spartalizumab as monotherapies is well characterized (see Section 1.1.1 and Section 1.1.2). This new combination has been proven to be safe at the dose of 400 mg BID capmatinib and spartalizumab 300 mg Q3W in HCC subjects treated in study [CINC280X2108] (see
Section 1.1.3.2). The 24 weeks follow-up of this run-in phase is intended not only to allow a thorough assessment of the safety profile of this new schedule but also to assess the preliminary efficacy of this combination before enrolling more subjects into the randomized part.
Appropriate eligibility criteria and stopping rules are included in this protocol. Recommended guidelines for prophylactic or supportive treatment for expected toxicities, including the management of study-drug induced AEs, (e.g. infusion reaction, pneumonitis) are provided in Section 6.5. The risk to subjects in this trial may be minimized by compliance with the eligibility criteria and study procedures, as well as by close clinical monitoring.
Oncology Clinical Trial Protocol (Version No. 00) Protocol No. CINC280D2201 As with any clinical study, there may be unforeseen risks with the combination studied, which could be serious. The specific risks for each compound are discussed below.

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

* Histologically confirmed locally advanced/metastatic (stage IIIB/IV) per AJCC/IASLC v.8) NCSCL
* EGFR wild-type, ALK rearrangement negative, NSCLC
* Subject has demonstrated progression following one prior platinum doublet and one prior PD-(L)1 checkpoint inhibitor (either alone or in combination, the most recent treatment regimen must have contained a PD-(L)1 checkpoint inhibitor)
* Subjects must be candidates for single agent docetaxel
* Subjects must have at least one lesion evaluable by RECIST 1.1

Exclusion criteria

* Prior treatment with a MET inhibitor or HGF (Hepatocyte growth factor) targeting
therapy
* Any untreated central nervous system (CNS) lesion
* Use of any live vaccines against infectious diseases within 12 weeks of initiation
of study treatment

Study design

Design

Study phase:	2
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):	14-05-2019
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	no name yet
Generic name:	capmatinib
Product type:	Medicine
Brand name:	no name yet
Generic name:	spartalizumab

Ethics review

Approved WMO Date:	18-12-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-03-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-10-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-03-2020

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2018-001420-19-NL
ClinicalTrials.gov	NCT03647488
CCMO	NL67932.091.18