OPEN-LABEL PHASE Ib/II, MULTICENTER STUDY OF THE COMBINATION OF RO5479599 WITH CARBOPLATIN AND PACLITAXEL IN PATIENTS WITH ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC) OF SQUAMOUS HISTOLOGY WHO HAVE NOT RECEIVED PRIOR CHEMOTHERAPY OR TARGETED THERAPY FOR NSCLC

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RO5479599 is an experimental drug under investigation by F. Hoffmann-La Roche for the treatment of solid tumors with a HER3 over-expressed, in this study focused on patients with advanced / metastatic non-small cell lung cancer (NSCLC) of squamous...

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

Summary

ID

NL-OMON41018

Source
ToetsingOnline

Brief title
BP29360

Condition

- Other condition
- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
cancer, squamous Non-Small Cell Lung Cancer

Health condition

gevorderde en/of gemetastaseerde sqNSCLC

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: F. Hoffmann La Roche Ltd.

Intervention

Keyword: HER3, Non-Small Cell Lung Cancer, RO5479599, Squamous

Outcome measures

Primary outcome

The primary objectives of this study are:

• To evaluate the safety and tolerability of RO5479599 in combination with

carboplatin and paclitaxel

• To estimate the efficacy of RO5479599 in combination with carboplatin and

paclitaxel, as measured by the objective response rate (ORR, defined as

complete response [CR] rate + partial response [PR] rate)

Secondary outcome

The secondary objectives of this study are:

• To evaluate patients for progression free survival (PFS) and overall survival

(OS)

• To evaluate disease control rate (DCR, defined as ORR + stable disease [SD] rate)

• To describe the pharmacokinetics (PK) of RO5479599 in combination with carboplatin and paclitaxel

The exploratory objectives for this study are:

• To evaluate heregulin (HRG) and HER3 expression levels, as well as other biomarkers related to HER signaling and the mechanism of action of RO5479599 in combination with carboplatin and paclitaxel, anti-tumor activity and potential mechanisms of resistance, in mandatory archival formalin-fixed paraffin-embedded tumor samples and/or fresh tumor biopsies obtained at screening and for (optional) tumor samples collected before study treatment and at disease progression

• To explore the relationship between tumor and immune-related biomarkers from blood and tissue and clinical outcome

• To explore the relationship of HRG mRNA expression with clinical response

• To explore the relationship of plasma, salivary and sputum tumoral microRNA / mRNA expression with clinical response

• To describe the correlation between PK, PD results and clinical outcomes

Study description

Background summary

This is a scientific study of RO5479599, an agent that binds to the HER3 receptor of malignant tumors, resulting in tumor cell apoptosis. Preclinical

research has demonstrated antitumor effect of RO5479599; a greater anti-tumor effect was seen when the drug was used in combination with anti-EGFR therapy. This study of RO5479599 aims to gain insight into the action of the drug in combination with carboplatin and paclitaxel in patients with advanced or metastatic non-small cell lung cancer (NSCLC) of squamous histology.

Study objective

RO5479599 is an experimental drug under investigation by F. Hoffmann-La Roche for the treatment of solid tumors with a HER3 over-expressed, in this study focused on patients with advanced / metastatic non-small cell lung cancer (NSCLC) of squamous cell histology.

Study design

This is an open-label, multicenter, single-arm Phase Ib / II study of the combination of RO5479599 with Carboplatin and Paclitaxel in patients with advanced / metastatic non-small cell lung cancer (NSCLC) of squamous histology, who have not received prior chemotherapy or targeted therapy for NSCLC. The study consists of a Safety Run-In Phase followed by an Efficacy Phase. The study begins with a Safety Run-In Phase with a minimum of 10 and up to 20 evaluable patients. Patients will be treated with a fixed dose of 800 mg RO5479599, administered according to a Q3W schedule, plus Carboplatin and Paclitaxel as a standard of care. Patients will be observed for 6 weeks (i.e. during two treatment cycles bloedvalues and vital signs will be measured at certain timepoints, please refer to the schedual of assessments in the protocol for further information) in order to confirm the dose and schedule that will be used in the Efficacy Phase of the study. To demonstrate efficacy of the product about 33 patients will be observed in the Efficacy Phase of the study.

Intervention

Patients eligible for participation in this study are treated with RO5479599 and Carboplatin or Paclitaxel according to the study specific schedule as described on page 55/56 of the Protocol.

Study burden and risks

Until now there have been no major safety issues reported in patients who have received RO5479599. Animal studies previously performed also do not indicate adverse events associated with RO5479599. Animals showed inflammatory reactions against RO5479599. Based on preliminary results, such a reaction in humans is rare. Mainly during the first injection (and up to 24 hours) there is a risk of an Infusion Related Reaction (IRR) or an allergic reaction. The most common adverse events in clinical studies already carried out with RO5479599 are diarrhea, fatigue, loss of appetite, rash or dry skin, mucosal inflammation and

IRRs.
The test procedures and treatments may entail risks and cause discomfort. There is a slight chance of pain or a bruise when blood is collected. Some people may faint when blood is collected. During this study, with patient approval, biopsies may be performed. The following risks are associated with a biopsy: bruising, bleeding, infection and side-effects of the numbing medication (anaesthetic) that may be given for the procedure. In rare cases, these risks may be life-threatening and make hospitalization necessary. In order to reduce the risks, the site of the biopsy will be numbed and sterile techniques will be used.
Undergoing an MRI or PET / CT scan may entail additional discomfort, specifically, a sense of claustrophobia (being *locked in*) or suffering from the noise during the scan.
The disadvantages of participating in this study are: time investment to undergo various procedures for this study, additional or prolonged hospitalization(s), additional blood collection, additional examinations, biopsies and any side effects of RO5479599.

An allergic reaction to the study medication may be mild (skin rash, fever, chills, headache, nausea or vomiting) or severe (low blood pressure, elevated heart rate, anxiety and / or difficulty swallowing or breathing). These side-effects are most common during the first few doses, but may occur during any infusion. The research physician may prescribe medication and other supportive care in order to reduce or prevent the severity of these side-effects. In rare cases, these symptoms can be so severe that they possibly require the administration of RO5479599 to be stopped permanently.
Sometimes, side-effects develop and get worse over time due to the development of antibodies against the study medication. Usually these side-effects involve skin rashes, joint and muscle pain, fever and fatigue. Medication may be prescribed to reduce the effect of these symptoms. If these side-effects are serious or persist for a very long time, it may be necessary to permanently stop administration of RO5479599.
Studies with laboratory animals have not shown RO5479599 to affect cardiovascular tissue. Patients will be monitored closely during the study. For example, multiple electrocardiograms (ECGs) will be made.
Risk of drug interactions:
It is possible that treatment with RO5479599 may affect the activity of other medication.
Patient may experience one or more of these side-effects, or currently unknown side effects, and they may be mild, moderate, severe, or (in very rare cases) life-threatening or even fatal. If side-effects do occur, the study physician must be notified immediately. He / she may prescribe medication to combat any discomfort. Furthermore, in the event of a serious reaction, the study physician may decide to suspend or permanently terminate treatment with the study medication.

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

- Age> / = 18 years
- ECOG performance status (PS) 0 - 1
- Histologically confirmed squamous NSCLC patients
- Locally advanced or metastatic (stage IIIB or IV) squamous NSCLC
- No prior systemic chemotherapy, targeted therapy for metastatic NSCLC
- Evidence of at least one radiologically measurable lesion as per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Adequate hematological, liver and renal function
- Use of highly effective contraception

Exclusion criteria

- Concurrent therapy with any other investigational drug
- History or clinical evidence of central nervous system (CNS) primary tumors or metastases
- Evidence of significant, uncontrolled concomitant diseases, which could affect compliance with the protocol or interpretation of results, including uncontrolled diabetes mellitus and/or significant cardiovascular disease or uncontrolled infection
- Any other diseases, metabolic dysfunction, a physical examination finding or a clinical laboratory finding, giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
- Major surgery or significant traumatic injury <28 days prior to the first study treatment infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment
- Pregnant or breast-feeding women
- History of other malignancies that could affect compliance with protocol or interpretation of results. Patients with malignancies diagnosed more than five years prior to study day one, adequately treated carcinoma in situ of the cervix or basal or squamous cell skin cancer are generally eligible

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-11-2014
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Paraplatin

Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-08-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-12-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2014-001498-15-NL
Other	EudraCT: 2014-001498-15, Clinicaltrials.gov
CCMO	NL49820.031.14