Etude de phase 1 évaluant le RAD001 en association avec la radiothérapie dans les cancers bronchiques non à petites cellules

Published: 20-10-2009
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Primary objective: to evaluate the tolerability of the combination of RAD001 with radiotherapy.Secondary objective(s) To determine the antitumor activity of the combination of RAD001 (EVEROLIMUS) and radiotherapy (CR+PR+SD). To determine the...

Ethical review	Not approved
Status	Will not start
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON33139

Source
ToetsingOnline

Brief title
RAD001-RT

Condition

- Respiratory tract neoplasms

Synonym
lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut

Source(s) of monetary or material Support: Novartis,Novartis NL

Intervention

Keyword: RAD001 (everolimus) lung radiotherapy

Outcome measures

Primary outcome

Primary objective: to evaluate the tolerability of the combination of RAD001

with radiotherapy.

Secondary outcome

Secondary objective(s) To determine the antitumor activity of the combination

of RAD001 (EVEROLIMUS) and radiotherapy (CR+PR+SD). To determine the

progression-free survival and the overall survival.

Study description

Background summary

RAD001 is known as a radiosensitizer. In this study we want to evaluatie the tolerability of RAD001 (everolimus) when combined with radiotherapy in patients with Non-small cell lung cancer, stage IIIA/B.

Study objective

Primary objective: to evaluate the tolerability of the combination of RAD001 with radiotherapy.
Secondary objective(s) To determine the antitumor activity of the combination of RAD001 (EVEROLIMUS) and radiotherapy (CR+PR+SD). To determine the

progression-free survival and the overall survival.

Study design

First phase of the study:
RAD001 (everolimus) will be administered per os every Monday, one week before then during the radiotherapy and will be continued for 3.5 weeks after the end of the radiotherapy. Chemotherapy is given 4.5 weeks after the end of radiotherapy. Three patient cohorts are planned, receiving 10, 20 and 50 mg of RAD001 per week.
Second phase of the study:
RAD001 (everolimus) will be administered per os every day one week before then during the radiotherapy and will be continued for 3.5 weeks after the end of radiotherapy. Chemotherapy is given 4.5 weeks after the end of radiotherapy. Three patient cohorts are planned, receiving 2.5, 5 and 10 mg of RAD001 per day.
The two phases of the study may be conducted independently and in parallel.
Radiotherapy: 66 Grays over 6.5 weeks. (5 weekly fractions of 2 Grays)
Chemotherapy: 2 cycles: Cisplatin 100 mg/m2 D1, Navelbine 25 mg/m2 D1, D8, every 21 days.

Intervention

RAD001 in combination with standard radiotherapy.
Study treatments RAD001 (everolimus) combined with radiotherapy (66 Grays) and followed by chemotherapy: dose escalation of RAD001 according to two regimens

1- RAD001 (everolimus) administered per os every Monday, one week before then during the radiotherapy then for 3.5 weeks after the end of radiotherapy. Three patient cohorts are planned, receiving 10, 20 and 50 mg per week.

2- RAD001 (everolimus) will be administered per os every day one week before then during the radiotherapy then for 3.5 weeks after the end of radiotherapy. Three patient cohorts are planned, receiving 2.5, 5 and 10 mg per week.
Number of patients Calculation of the number of subjects required:
30

Study burden and risks

the burden associated with participation in this trial is not totally different from standart treatment with chemoradiation. After screening patients will be seen every week by their radiation-oncologist to check for complaints related to the radiotherapy or related to the study medication. The only extra examination will be a weekly electrocardiogram. Since this is a phase I trial we don't know the side effects. From the experience with RAD001 alone mild side effects can be expected such as fatique, nausea and/or vomiting, mouth ulcers, skin rash and headache. A few cases of moderate non-infectious pulmonary

toxicity have been reported. It is usually of moderate intensity and regresses on withdrawal of the treatment. In less then 1 % a severe form has been reported. Therefore the physician will carefully watch for unusual respiratory symptoms such as sudden onset of breathing difficulties, cough or fever.

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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

1) Unresectable non-small cell lung cancer, stage IIIA/B, or stage IV for which the primary tumor is symptomatic (cough, dyspnea, pain) without extra-thoracic lesions rapidly evolving

2) Measurable lesion, documented histologically, potentially accessible during fiberoptic bronchoscopy.
3) Age > 18 years, WHO 0-1,
4) Neutrophil count > 1500 /mm3, Hemoglobin > 9 g/dL, Platelet count > 100,000/mm3
5) Bilirubin < 1.5 mg/dL, Transaminases < 3 N, albumin >30 g / L, PT > 70%
6) Creatinine < 120 µM/L
7) Patient information and informed consent form signed.
8) No previous treatment for lung cancer (surgery, radiotherapy, chemotherapy).

Exclusion criteria

1) Patients previously treated with RAD001 (everolimus) or any other mTOR inhibitor
2) Stage IV for which the primary tumor is not symptomatic with extra-thoracic lesions rapidly evolving requiring systemic treatment
3) Previous radiotherapy,
4) Venous or arterial thrombosis, pulmonary embolism during the previous six months
5) Concomitant treatment with phenytoin, phenobarbital or any other antiepileptic agent, history of epilepsy
6) Concomitant treatment with medicinal products that inhibit, induce or are substrates for CYP3A4

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-10-2009
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Rad001
Generic name:	everolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-10-2009
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Not approved Date:	25-11-2009
Application type:	First submission
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	EUCTR2007-001698-27-NL
CCMO	NL29207.031.09