A randomized, double-blind placebo-controlled, multicenter phase III study in patients with advanced carcinoid tumor receiving Sandostatin LAR and RAD001 10 mg/Day or Sandostatin LAR and Placebo

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To determine whether treatment with RAD001 10 mg/d plus Sandostatin LAR® prolongs the progression free survival (PFS) compared to treatment with Sandostatin LAR® alone in patients with advanced carcinoid tumor.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine and glandular disorders NEC
Study type	Interventional

Summary

ID

NL-OMON37069

Source
ToetsingOnline

Brief title
RAD001 and Sandostatin LAR in patients with advanced carcinoid tumor

Condition

- Endocrine and glandular disorders NEC

Synonym
Carcinoid

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Advanced, Carcinoid, RAD001, Sandostatin LAR

Outcome measures

Primary outcome

The primary objective is to compare the progression-free survival (based on the central radiological assessment). The primary efficacy variable progression-free survival will be analyzed using both Intention to Treat (ITT) and per protocol population. The analysis result of the ITT population using the central radiological assessment is considered as the primary analysis.

Secondary outcome

Secondary efficacy variables include best overall response rate, the duration of overall response (CR or PR) and of overall complete response (CR), overall survival and otherefficacy markers. Best overall response rate will be assessed by RECIST criteria.

Study description

Background summary

Low grade neuroendocrine carcinoma consists of carcinoid and pancreatic endocrine tumors
A recent increase in the incidence of carcinoid tumors have been detected. These tumors originate from the neuroendocrine cells throughout the body and are capable of producing various peptides. Their clinical course is often

indolent but can also be highly aggressive and resistant to therapy. Current treatments for metastatic tumors have either low biologic activity, high unfavorable toxicity profile or both.

For carcinoid, despite the many chemotherapy trials that have been conducted, no regimen has demonstrated a response rate of more than 15%. Interferon has also been widely studied in this disease. While octreotide has a role in the management of carcinoid syndrome, objective tumor responses are rare.

RAD001 has a potential to act directly on the tumor cells by inhibiting tumor cell growth anad proliferation. On the other hand RAD001 has also a potential to act indirectly by inhibiting angiogenesis leading to reduced tumor vascularity.

Study objective

To determine whether treatment with RAD001 10 mg/d plus Sandostatin LAR® prolongs the progression free survival (PFS) compared to treatment with Sandostatin LAR® alone in patients with advanced carcinoid tumor.

Study design

This is a prospective, randomized, double-blind, multicenter, placebo-controlled, parallel group phase III study to evaluate the safety and efficacy of RAD001 10 mg/day or matching placebo plus Sandostatin LAR® in patients with advanced carcinoid tumor.

Intervention

Treatment arm 1: RAD001 (everolimus) 10 mg/d along with Sandostatin LAR® Depot 30mg every 28 days

Treatment arm 2: Placebo along with Sandostatin LAR® Depot 30mg every 28 days

Study burden and risks

Toxicity of RAD001 alone or of the combination of RAD001 and Sandostatine LAR.
Radiation exposure of CT-scans.
Obtaining blood samples may cause some discomfort, bruising, bleeding from the site of sampling, formation of a blood clot, and, in rare cases, infection.

Contacts

Public

Novartis

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Scientific
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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. Advanced (unresectable or metastatic) biopsy-proven carcinoid tumor.
2. Confirmed low-grade or intermediate-grade neuroendocrine carcinoma
3. Radiological documentation of progression of disease within 12 months prior to randomization
4. Measurable disease CTscan or MRI
5. Adequate bone marrow function (ANC * 1.5 x 109/L, Platelets * 100 x 109/L, Hb >9 g/dL)
6. Adequate liver function:
* serum bilirubin * 1.5 x ULN
* INR < 1.3 x ULN (or < 3 on anticoagulants)
* ALT and AST * 2.5x ULN (* 5x ULN in patients with liver metastases)
7. Adequate renal function: serum creatinine * 1.5 x ULN
8. Fasting serum cholesterol *300 mg/dL OR 7.75 mmol/L AND fasting triglycerides * 2.5 x ULN. Treatment with lipid lowering agents is allowed.
9. WHO performance 0-2

Exclusion criteria

1. Patients with poorly differentiated neuroendocrine carcinoma, high-grade neuroendocrine carcinoma, adenocarcinoid, goblet cell carcinoid and small cell carcinoma
2. Cytotoxic chemotherapy, immunotherapy or radiotherapy < 4 weeks prior to randomization
3. Received treatment with Sandostatin LAR® Depot or any other long-acting somatostatin analog < 2 weeks prior to randomization.
4. Hepatic artery embolization < the last 6 months (1 month if there are other sites of measurable disease), or cryoablation of hepatic metastasis < 2 months of randomization
5. Prior therapy with mTOR inhibitors (sirolimus, temsirolimus, everolimus)
6. Uncontrolled diabetes mellitus (fasting serum glucose >1.5 X ULN)
7. Severe and/or uncontrolled medical conditions such as:
* unstable angina pectoris, symptomatic congestive heart failure, myocardial infarction
* 6 months prior to randomization, serious cardiac arrhythmia,
* severe infection
* cirrhosis, chronic (active) hepatitis
* severely impaired lung function
8. Chronic treatment with corticosteroids or another immunosuppressive agent
9. Patients with a known history of HIV seropositivity
10. Patients with an active, bleeding diathesis
11. History of another primary malignancy * 3 years, except non-melanoma skin cancer, and carcinoma in situ of uterine cervix

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	12-06-2007
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet geregistreerd voor deze indicatie
Generic name:	everolimus
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Sandostatin LAR
Generic name:	octreotide depot
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-03-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-03-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-08-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-04-2011
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-07-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-08-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-08-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2006-004507-18-NL
ClinicalTrials.gov	NCT00412061
CCMO	NL16050.042.07