Open-Label Multicenter 2-Arm Phase I Study of RO5429083 with Dose-Escalation and Extension Cohorts, and Imaging Cohorts with RO5429083 and 89Zr-labeled RO5429083, in Patients with Metastatic and/or Locally Advanced, CD44-Expressing, Malignant Solid Tumors

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Arm A-Dose Escalation CohortPrimary Objectives* To describe the pharmacokinetics (PK) and safety profiles (including the maximum tolerated dose (MTD) or Optimal Biological Dose) of escalating doses of RO5429083 in patients with metastatic and/or...

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

Summary

ID

NL-OMON39242

Source
ToetsingOnline

Brief title
BP25385

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
different types of malignant tumors, solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Roche Nederland BV

Intervention

Keyword: CD44, Phase I, solid tumors

Outcome measures

Primary outcome

Arm A-Dose Escalation Cohort

Primary Objectives

* To describe the pharmacokinetics (PK) and safety profiles (including the maximum tolerated dose (MTD) or Optimal Biological Dose) of escalating doses of RO5429083 in patients with metastatic and/or locally advanced malignant CD44-expressing solid tumors.

Arm A-Extension Cohort

Primary Objectives

• To investigate the Tumor Growth Control Rate (TGCR): complete response (CR), partial response (PR), and stable disease (SD).

• To describe the safety profile of RO5429083 in patients with metastatic and/or locally advanced malignant CD44-expressing solid tumors.

• To determine the recommended Phase II dose.

Arm B: Imaging Study with 89Zr labeled RO5429083

Primary Objectives

• To evaluate the in vivo biodistribution and organ pharmacokinetics of 89Zr labeled RO5429083 in patients with CD44-expressing solid tumors.

Secondary outcome

Arm A-Dose Escalation Cohort

Secondary Objectives

• To determine the recommended dose (RD) for RO5429083 for the extension cohort.

• To describe the anti-tumor activity of RO5429083.

• To describe the pharmacodynamic effects of RO5429083 in skin biopsies, whole blood samples and tumor biopsies.

Arm A-Extension Cohort

Secondary Objectives

• To describe the anti-tumor activity of RO5429083 using:

o Objective Response Rate (ORR)

o Duration of Response

o Progression Free Survival

• To describe the PK profile of RO5429083.

• To describe the pharmacodynamic effects of RO5429083 in skin biopsies, whole

blood samples and tumor biopsies.

Arm B: Imaging Study with 89Zr labeled RO5429083

Secondary Objectives

• To explore target saturation and correlate with pharmacological effect.

Study description

Background summary

Cancer remains a major cause of mortality and morbidity worldwide despite recent progress with drugs providing survival benefit to patients. For most solid tumors and for many hematologic malignancies, the risk for the development of metastases and the rate of tumor recurrence are substantial. Therefore, the medical need for new, effective, and safe treatments of malignant diseases remains high.
It is widely reported that hyaluronan-CD44 interactions are important in both malignancy and resistance to therapy. Prevalence data with human tumor samples further supports the clinical evaluation in various solid tumors and hematological malignancies

Study objective

Arm A-Dose Escalation Cohort
Primary Objectives
* To describe the pharmacokinetics (PK) and safety profiles (including the maximum tolerated dose (MTD) or Optimal Biological Dose) of escalating doses of RO5429083 in patients with metastatic and/or locally advanced malignant CD44-expressing solid tumors.

Arm A-Extension Cohort
Primary Objectives
• To investigate the Tumor Growth Control Rate (TGCR): complete response (CR), partial response (PR), and stable disease (SD).
• To describe the safety profile of RO5429083 in patients with metastatic and/or locally advanced malignant CD44-expressing solid tumors.
• To determine the recommended Phase II dose.

Arm B: Imaging Study with 89Zr labeled RO5429083
Primary Objectives
• To evaluate the in vivo biodistribution and organ pharmacokinetics of 89Zr labeled RO5429083 in patients with CD44-expressing solid tumors.

Study design

This is a first in human, open-label, multicenter, Phase I clinical study of RO5429083 and 89Zr labeled RO5429083. The study will be conducted with two arms. Arm A will be a dose-escalation schedule with an extension cohort which will seek to evaluate the PK, safety, recommended Phase II dose, and efficacy of RO5429083 in patients with metastatic and/or locally advanced malignant CD44-expressing solid tumors. Arm B will be performed at VUmc in the Netherlands. Arm B will explore body distribution and kinetics using PET with 89 Zr labeled RO5429083 in CD44-expressing patients with advanced squamous cell carcinoma of the head and neck as well as squamous cell carcinoma of the esophagus with an option to add other indications if needed.

Intervention

Arm A will be a multi-center standard *3+3* design and will consist of cohorts of a minimum of 3 patients which will be sequentially enrolled in one of the dose levels of RO5429083 administered intravenous on a q2W (defined as 1 dose of RO5429083 followed by 13 days without treatment every 2 weeks; 1 cycle = 2 weeks) schedule. Dose-escalation will be based on the safety evaluation of patients after two cycles (q2W x 2) at each dose level

Arm B: 89Zr-labeled RO5429083 will be administered intravenously.

Study burden and risks

There is the risk of slight pain, bruising or infection when your blood is drawn. Drawing blood may cause some people to faint.
Having a CT, MRI or PET scan may mean some added discomfort to you. In particular, you may be bothered by feelings of claustrophobia and the noise during the test.
The glue used to keep the electrodes in place during the ECG may irritate your skin and cause redness.

This is the first research study to use RO5429083 in patients currently. No new information about possible side effects of RO5429083 in patients has been found other than already formulated upfront the study (based on similar antibody products).

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

- Adult patients, >/= 18 years of age;- Metastatic and/or locally advanced malignant CD44-expressing solid tumors (Arm A);- Histologically confirmed metastatic and/or locally advanced malignant CD44-expressing solid tumors ;- Patients with disease progression on standard therapy, or have tumors that are not curable by standard therapy;- Life expectancy of over 12 weeks

Exclusion criteria

- Concurrent therapy with any other investigational drug;- Known or suspected CNS metastases including leptomeningeal metastases;- Active bleeding, bleeding diathesis or history of coagulation disorder;- Uncontrolled diabetes mellitus;- Active or uncontrolled

infections;- Patients with HIV infections;- Patients with poorly controlled hypertension

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):	07-06-2011
Enrollment:	43
Type:	Actual

Ethics review

Approved WMO Date:	21-03-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2011
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2013
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	BP25385
EudraCT	EUCTR2010-021168-13-NL
CCMO	NL35263.029.11