An open-label, multi-center, expanded access study of RAD001 in patients with metastatic carcinoma of the kidney who are intolerant of or have progressed despite any available vascular endothelial growth factor receptor tyrosine kinase inhibitor therapy

Published: 07-01-2009
Last updated: 06-05-2024

The primary objective of the study is to evaluate additional safety of RAD001 in patients with MRCC who are intolerant of or whose disease has progressed despite any available prior VEGF receptor tyrosine kinaseinhibitor therapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON33782

Source
ToetsingOnline

Brief title
PhIIIb, open label RAD001 EAP in mRCC

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
metastatic kidney cancer / metastatic renal cell carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: expanded access, Metastatic renal cell carcinoma, non-responsive to VEGF receptor TKI treatment, RAD001

Outcome measures

Primary outcome

Grade 3/4 adverse events and serious adverse events will be captured

Secondary outcome

Tumor response and progression will be assessed using RECIST Criteria.Tumor assessments of measurable (CT scan/MRI) disease/lesions will be performed at screening and repeated every 3 months for the first year and then every 6 months thereafter, and at discontinuation of the study drug. Lesion size and measurements will not be collected; however, the Investigator*s best overall response will be captured.

After the administration of the last dose of RAD001 or RAD001 becomes commercially available, no further AEs/SAEs or survival data will be collected after the required 28 day safety interval.

Study description

Background summary

RAD001 (everolimus, an mTOR inhibitor) is an oral derivative of rapamycin. and was approved in 2003 in Europe (trade name: Certican®) for the prevention of organ rejection in patients with renal and cardiac transplantation. RAD001 is also being investigated as an anticancer agent based on its potential to act directly on the tumor cells by inhibiting tumor cell growth and proliferation and indirectly by inhibiting angiogenesis via potent inhibition of tumor cell HIF-1 activity and VEGF production and VEGF-induced proliferation of endothelial cells. At weekly and daily schedules and at various doses explored RAD001 has been generally well tolerated. The most frequent adverse events (rash, mucositis, fatigue and headache) associated with RAD001 have been manageable. Non-infectious pneumonitis has been reported with mTOR inhibitors but is commonly low-grade and reversible with RAD001.
Novartis has filed an NDA in MRCC in EU and US as of June 2008. There are no other agents with demonstrated efficacy in this disease setting. Based on the results of the Phase III pivotal registration study, this expanded access protocol is designed to fulfill an unmet medical need by providing RAD001 to patients who are without satisfactory
treatment alternatives.

Study objective

The primary objective of the study is to evaluate additional safety of RAD001 in patients with MRCC who are intolerant of or whose disease has progressed despite any available prior VEGF receptor tyrosine kinase
inhibitor therapy.

Study design

This is an open-label, multi-center protocol designed to evaluate additional safety of RAD001 and to make RAD001 available to patients with MRCC who are intolerant of or whose disease has progressed on any available VEGF receptor tyrosine kinase inhibitor therapy. No other agents have demonstrated efficacy in this disease setting. Safety data will fulfill
international regulatory requirements.
All patients will be screened for inclusion and exclusion criteria within five weeks prior to the first dose of RAD001. See Table 7-1 of the protocol for a description of the screening evaluations required.
Baseline evaluations will be performed within two weeks of the first dose of RAD001. See Table 7-1 of the protocol for a description of the baseline evaluations required.
Subsequently, patients will be asked to visit the clinic monthly thereafter.
For purposes of this study each cycle will be 28 days and study drug will be administered continuously.

Intervention

A daily, oral dose of 10 mg RAD001 will be administered continuously from start until either progression of disease, unacceptable toxicity, death, discontinuation from study from any other reason, or until the drug becomes commercially available for MRCC in each participating country or until 15 Juni 2010, whichever occurs first.

Study burden and risks

Apart from a pregnancy test, if applicable, and a request to use barrier contraceptives, if applicable, extra invasive procedures outside the routine care for this patient group are not requested. The additional risks associated with participation in this study, in view of the general condition of the target population and the lack of alternative treatment options, are considered to be low.

Contacts

Public
Novartis

Postbus 241
6800 LZ Arnhem
Nederland
Scientific
Novartis

Postbus 241
6800 LZ Arnhem
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

• Age >= 18 years old.
• Patients with histologically or cytologically confirmed metastatic renal cell carcinoma.
• Patients who are intolerant of or have progression on or after stopping treatment with any available VEGF receptor tyrosine kinase inhibitor therapy.
• Prior vaccine therapy or treatment with cytokines (i.e., IL-2, Interferon) and/or VEGF-ligand inhibitors (i.e., bevacizumab) is permitted.
• Patients with measurable or non-measurable disease by RECIST criteria.
• Patients with history of another distinguishable malignancy (such as nonmelanoma skin cancer, or low grade lymphoma, or CLL, or well controlled low grade prostate cancer), which are neither life threatening nor require chemotherapy or radiation.
• Patients with history of brain metastasis who are neurologically stable following definitive radiation or surgery and do not require corticosteroids.
• Patients with a Karnofsky Performance Status >=70%.
• Patients with adequate bone marrow function defined as ANC >= 1.5 x 109/L, Platelets >= 100 x 109/L, Hgb >9 g/dL.
• Patients with adequate liver function defined as serum bilirubin <= 1.5 x ULN, ALT and AST <= 2.5x ULN. Patients with known liver metastases who have an AST and ALT <= 5x ULN.
• Patients with adequate renal function defined as serum creatinine <= 2 x ULN.
• Women of childbearing potential must have had a negative serum or urine pregnancy test within 14 days prior to the administration of study drug.
• Patients must give written informed consent according to local guidelines.

Exclusion criteria

• Patients receiving chemotherapy, immunotherapy, radio-therapy or any other investigational agent (including pazopanib) within 4 weeks of study entry, or sunitinib and/or sorafenib within 1 week of the first dose of RAD001.
• Patients who have previously received RAD001 or other mTOR inhibitors.
• Patients with a known hypersensitivity to RAD001 or other rapamycin analogs (sirolimus, temsirolimus), or to its excipients.
• Patients receiving systemic treatment with corticosteroids or another immunosuppressive agent. Patients may receive low dose treatment of corticosteroids with a maximum dose of 20 mg prednisone or 10 mg dexamethasone per day, if they are being given for disorders such as

rheumatoid arthritis, asthma, or adrenal insufficiency. Topical or inhaled corticosteroids are permitted.
• Patients with an active bleeding diathesis.
• Patients who have undergone major surgery within 4 weeks prior to starting study drug (e.g., intra-thoracic, intra-abdominal, or intra-pelvic), open biopsy, or significant traumatic injury, or who have not recovered from the side effects of any of the above.
• Patients with any severe and/or uncontrolled medical conditions such as unstable angina pectoris, symptomatic congestive heart failure, myocardial infarction <= 6 months, serious uncontrolled cardiac arrhythmia, uncontrolled hyperlipidemia, active or uncontrolled severe infection, cirrhosis, chronic or persistent active hepatitis or severely impaired lung function.
• Uncontrolled diabetes (fasting glucose > 2x ULN)
• Female patients who are pregnant or breast feeding, or adults of reproductive potential who are not using effective birth control methods. If barrier contraceptives are used, they must be continued throughout the study by both sexes.
• Patients unwilling to or unable to comply with the protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-03-2009
Enrollment:	42
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	07-01-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	24-02-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-07-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-08-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2007-005460-28-NL
ClinicalTrials.gov	NCT00655252
CCMO	NL24639.058.08