A phase Ib/II study investigating the combination of RAD001 with trastuzumab and paclitaxel in patients with HER2-overexpressing metastatic breast cancer.

Published: 28-11-2008
Last updated: 06-05-2024

To evaluate the efficacy of the dose level/regimen(s) of RAD001recommended from the phase I with HT therapy. This will bebased on the evaluation of overall response rate according toRECIST [Post-Text Supplement 1].

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

Summary

ID

NL-OMON35692

Source
ToetsingOnline

Brief title
HER2+ MBC, RAD001 + trastuzumab+ paclitaxel.

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis

Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Keyword: HER2-positive, metastatic breastcancer, RAD001

Outcome measures

Primary outcome

To evaluate the efficacy of the dose level/regimen(s) of RAD001

recommended from the phase I with HT therapy. This will be

based on the evaluation of overall response rate according to

RECIST [Post-Text Supplement 1].

Secondary outcome

To evaluate Progression Free Survival (PFS)

To evaluate the Time To Progression (TTP)

To evaluate overall survival (OS)

To describe the safety profile of the studied recommended dose

level/regimen(s)

Study description

Background summary

Weekly paclitaxel in combination with trastuzumab has been studied in HER2-positive patients with previously treated, as well as previously untreated metastatic breast cancer, and has demonstrated response rates between 56% and 81% with a low incidence of grade 3-4 toxicities.
The optimal duration of trastuzumab therapy is currently not known but there is emerging evidence that suggests that continuing trastuzumab treatment even after progression of the disease, while changing the chemotherapy partner, may produce clinical benefit.
Preclinical rationale is established for the combination of an mTOR

inhibitor with trastuzumab; loss of PTEN predicts resistance to trastuzumab.
Evidence that inhibition of the mTOR pathway can enhance efficacy of paclitaxel has been shown with the RAD001 in preclinical models.
RAD001 (everolimus), a derivative of rapamycin, is a signal transduction inhibitor that acts by selectively inhibiting mTOR (mammalian target of rapamycin), a serine-threonine kinase implicated in the P13/AKT pathway and essential for the regulation of cell growth and proliferation in many cell systems.
Pre-clinical investigations have demonstrated that RAD001 is a potent inhibitor of the proliferation of a range of human tumor cell lines in vitro and inhibits tumor growth in vivo in a range of animal models.
RAD001 is currently being evaluated in clinical trials both as a monotherapy and in combination with other anti-cancer agents. Early results show that RAD001 is generally well tolerated and that single agent therapy may induce prolonged disease stabilization and even tumor regressions in a subset of patients.

Study objective

To evaluate the efficacy of the dose level/regimen(s) of RAD001 recommended from the phase I with HT therapy. This will be based on the evaluation of overall response rate according to RECIST [Post-Text Supplement 1].

Study design

In phase II a 10 mg daily RAD001 continuous regimen will be used. (Only one arm will be used).

Treatment will be repeated every 28 days for at least 6 cycles unless there is evidence of progression or occurrence of unacceptable toxicities. Following completion of chemotherapy (or early discontinuation of chemotherapy), patients may continue to receive RAD001 on a daily or weekly basis along with trastuzumab or alone (if trastuzumab is discontinued early for toxicity), until progressive disease or unacceptable toxicity occurs.

Intervention

Patients will be instructed to use RAD001 10 mg daily dose. Tablets contain 2,5 / 5 / 10 mg each.

Study burden and risks

After the screeningsperiod patients have to visit the hospital once every week

during the first 6 cycles. (Core phase).
After 6 cycles the extension phase of the study starts for patients who have not yet progressive disease. During the extension phase patients have to visit the hospital on day 1, 8, and 15 of each cycle (cycle is 21 days).
Tumor evaluation will be done every 8 weeks during the core phase and every 9 weeks during the extension phase.
Use of RAD001 might cause side effects.

Contacts

Public
Novartis

Raapopseweg 1
6824 DP Arnhem
NL
Scientific
Novartis

Raapopseweg 1
6824 DP Arnhem
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Patients with histologically confirmed diagnosis of metastatic breast cancer demonstrating HER2-overexpression.
* Patients must have progressive disease on therapy or within 3 months of the last

trastuzumab dose for advanced disease OR recurrence within 12 months of completing trastuzumab-based therapy as (neo) adjuvant therapy.
* Patients may have received adjuvant chemotherapy and one or more prior chemotherapies for advanced disease.

Exclusion criteria

* Patients receiving endocrine therapy for breast cancer < 2 weeks prior to study treatment start (endocrine therapy must have either failed in patients with hormone receptor positive disease or patients must be considered unsuitable for endocrine therapy).
* Patients who received chemotherapy, immunotherapy or radiotherapy within 4 weeks prior to study treatment start or patients who have received lapatinib < 2 weeks prior to study treatment start.
* Patients who have previously received mTOR inhibitors.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2009
Enrollment:	5
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:	28-11-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-02-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-09-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-10-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-12-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-03-2010
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-07-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-06-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	31-07-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	EUCTR2006-001596-37-NL
ClinicalTrials.gov	NCT00426556
CCMO	NL25462.068.08