An open-label, multi-center, expanded access study for postmenopausal women with estrogen receptor positive locally advanced or metastatic breast cancer who have progressed following prior endocrine therapy, investigating the treatment of everolimus (RAD001) in combination with exemestane

Published: 23-03-2012
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Primary objective: to evaluate safety of everolimus in postmenopausal women with estrogen receptor positive locally advanced or metastatic breast cancer that is refractory to NSAIs.Secondary objective: to evaluate adverse events grade 3 and 4 in the…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON37575

Source
ToetsingOnline

Brief title
CRAD001YIC04

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: advanced, breast cancer, everolimus, exemestane

Outcome measures

Primary outcome

The number and percentage of patients having any adverse events (CTCAE, version 4.03).

Secondary outcome

Number and percentage of patients having any drug-related adverse events that is recorded as Grade 3 or 4 or as serious adverse event. 2: The number and percentage of patients having any adverse events related to concomitant treatment with zoledronic acid RTU formulation.

Study description

Background summary

There are no treatments for breast cancer specifically approved after recurrence or progression on a non-steroidal aromatase inhibitor (NSAI). Available options are based on common clinical practice and several treatment guidelines. The activity of exemestane in MBC after failure of NSAI was evaluated in a phase II trial. In 2011 the BOLERO-2 trial reported a significant benefit for hormone-receptor positive HER2-negative postmenopausal pretreated women in the advanced breast cancer setting by combining everolimus

with a standard endocrine treatment. Based on these positive results an NDA in EU and USA has been filed.
The purpose of this expanded access study is to establish additional safety data of everolimus (RAD001) in this patient population and to provide access to everolimus (RAD001) to patients who are without satisfactory treatment alternatives, until the drug is locally reimbursed for this indication or until 31 January 2014, whichever comes first.
In this study everolimus will be administered in combination with exemestane, which is an irreversible steroidal aromatase inactivator that has demonstrated efficacy in the treatment of postmenopausal patients with advanced BC.
Exemestane is indicated for adjuvant treatment of postmenopausal women with ER+ early BC who have received two to three years of tamoxifen and are switched to exemestane for completion of a total of five consecutive years of adjuvant hormonal therapy. It is also indicated for the treatment of advanced breast cancer in postmenopausal women whose disease has progressed following anti-estrogen therapy.

Study objective

Primary objective: to evaluate safety of everolimus in postmenopausal women with estrogen receptor positive locally advanced or metastatic breast cancer that is refractory to NSAIs.
Secondary objective: to evaluate adverse events grade 3 and 4 in the routine practice.
Secondary exploratory objective: to explore the tolerability of the concomitant treatment of zoledronic acid RTU (Ready To Use formulation) in the patients who will receive this treatment according to the clinical practice.

Study design

Open-label, non-comparative phase IIIb expanded access study. After written informed consent and screening, suitable patients will be treated with 10 mg everolimus once daily plus 25 mg exemestane once daily until disease progression, unacceptable adverse effects or until the drug is reimbursed in the Netherlands for this indication or until 31 January 2014, whichever comes first.
Study visits after 1, 2 and 3 months and every 2 months thereafter.
Up to 2200 patients will be enrolled.

Intervention

Treatment with everolimus plus exemestane.

Study burden and risks

Risk: Adverse events of study medication.

Burden:
Study visits after 1, 2 and 3 months and every 2 months thereafter.
Blood draws 45 ml/visit; every visit (fasting)
No grapefruit, citrus fruit and juices.
Other assessments according to regular treatment.

Contacts

Public
Novartis Pharma BV

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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.Adult women (* 18 years of age) with metastatic or locally advanced breast cancer not amenable to curative treatment by surgery or radiotherapy. ;2.Histological or cytological confirmation of estrogen-receptor positive (ER+) breast cancer;3.Postmenopausal women. Postmenopausal status is defined either by:;*Age * 55 years and one year or more of amenorrhea;*Age < 55 years and one year or more of amenorrhea, with an estradiol assay <

20 pg/ml ;*Surgical menopause with bilateral oophorectomy ;Note: Ovarian radiation or treatment with a luteinizing hormone-releasing hormone (LH-RH) agonist (goserelin acetate or leuprolide acetate) is not permitted for induction of ovarian suppression. ;4.Disease refractory to NSAI, defined as: ;a. Recurrence while on or within 12 months of end of adjuvant treatment with letrozole or anastrozole, or;b. Progression while on or within one month of end of letrozole or anastrozole treatment for advanced BC ;5.Adequate bone marrow and coagulation function as shown by:;*Absolute neutrophil count (ANC) * 1.5 109/L;*Platelets * 100 ×109/L;*Hemoglobin (Hgb) * 9.0 g/dL;*INR * 2 ;6.Adequate liver function as shown by:;*Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) * 2.5 ULN (or * 5 if hepatic metastases are present);*Total serum bilirubin * 1.5 × ULN (* 3 × ULN for patients known to have Gilbert Syndrome) ;7.Adequate renal function as shown by:;*Serum creatinine * 1.5 × ULN;8.Fasting serum cholesterol * 300 mg/dl or 7.75 mmol/L and fasting triglycerides * 2.5 × ULN

Exclusion criteria

1.HER2-overexpressing patients by local laboratory testing (IHC 3+ staining or in situ hybridization positive).;2.Previous treatment with exemestane or mTOR inhibitors. Except for the treatment with exemestane in the adjuvant setting providing patient remained disease-free for at least one year following completion.;3.Known hypersensitivity to mTOR inhibitors, e.g. sirolimus (rapamycin).;4.Patients receiving concomitant immunosuppressive agents or chronic corticosteroids use, at the time of study entry except in cases outlined below: ;Topical applications, inhaled sprays, eye drops or local injections are allowed. ;Patients on stable low dose of corticosteroids for at least two weeks before enrollment are allowed in case of treatment of brain metastases .;5.Bilateral diffuse lymphangitic carcinomatosis or metastasis of the lung as the only manifestation of disease (>50% of lung involvement), evidence of metastases estimated as more than a third of the liver as defined by sonogram and/or CT scan.;6.Patients with a known history of HIV seropositivity. ;7.Active, bleeding diathesis, or on oral anti-vitamin K medication (except low dose warfarin and acetylsalicylic acid or equivalent, as long as the INR is * 2.0);8.Any severe and / or uncontrolled medical conditions such as:;*Uncontrolled diabetes as defined by fasting serum glucose > 1.5 × ULN;*Acute and chronic, active infectious disorders and nonmalignant medical illnesses that are uncontrolled or whose control may be jeopardized by the complications of this study therapy;*Significant symptomatic deterioration of lung function. If clinically indicated, pulmonary function tests including measures of predicted lung volumes, DLco, O2 saturation at rest on room air should be considered to exclude restrictive pulmonary disease, pneumonitis or pulmonary infiltrates. ;9.Patients who test positive for hepatitis B or C (Patients who test negative for HBV-DNA, HBsAg, and HBcAb but positive for HBsAb with prior history of vaccination against Hepatitis B will be eligible)

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):	05-07-2012
Enrollment:	180
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Afinitor
Generic name:	everolimus
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Aromasin
Generic name:	exemesane
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	19-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2012
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	Clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-000073-23-NL
CCMO	NL40117.029.12