A PHASE III, DOUBLE-BLIND, PLACEBO CONTROLLED, RANDOMIZED STUDY OF TASELISIB PLUS FULVESTRANT VERSUS PLACEBO PLUS FULVESTRANT IN POSTMENOPAUSAL WOMEN WITH ESTROGEN RECEPTOR POSITIVE AND HER2 NEGATIVE LOCALLY ADVANCED OR METASTATIC BREAST CANCER WHO HAVE DISEASE RECURRRENCE OR PROGRESSION DURING OR AFTER AROMATASE INHIBITOR THERAPY

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To evaluate the efficacy, safety, pharmacology, and patient-reported outcomes of the combination of taselisib plus fulvestrant compared to placebo plus fulvestrant in ER+, HER2- postmenopausal women with locally advanced or MBC and who have had...

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

Summary

ID

NL-OMON45216

Source
ToetsingOnline

Brief title
GO29058

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast Cancer, mammacarcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Breast cancer, PIK3CA, Postmenopausal women

Outcome measures

Primary outcome

To compare the efficacy between taselisib + fulvestrant versus placebo +

fulvestrant as measured by investigator-assessed PFS in patients with

PIK3CA-mutant tumors

Secondary outcome

- To compare the overall objective response rate (ORR) between taselisib +

fulvestrant versus placebo + fulvestrant in patients with PIK3CA-mutant tumors,

on the basis of tumor assessments made by the investigator

- To compare the efficacy between taselisib + fulvestrant versus placebo +

fulvestrant as measured by OS in patients with PIK3CA-mutant tumors

- To estimate the duration of objective response (DOR) within taselisib +

fulvestrant versus placebo + fulvestrant in patients with PIK3CA-mutant tumors,

on the basis of tumor assessments made by the investigator

- To compare the clinical benefit rate (CBR) between taselisib + fulvestrant

versus placebo + fulvestrant in patients with PIK3CA-mutant tumors, on the

basis of tumor assessments made by the investigator

- To compare the efficacy between taselisib + fulvestrant versus placebo +

fulvestrant as measured by PFS determined by blinded independent central review

(BICR) in patients with PIK3CA-mutant tumors

Study description

Background summary

Not all ER+ breast cancers respond optimally to endocrine therapy.
Hyperactivation of the PI3K/AKT/mTOR signaling pathway was proven to promote both de novo and acquired resistence to hormone therapy. This supports the hypothesis that blocking PI3K/AKT/mTOR pathway signaling may have a therapeutic benefit in patients with Er+, HER2-negative breast cancer.

Study objective

To evaluate the efficacy, safety, pharmacology, and patient-reported outcomes of the combination of taselisib plus fulvestrant compared to placebo plus fulvestrant in ER+, HER2- postmenopausal women with locally advanced or MBC and who have had recurrence or progression of diasesa on or after administration of an aromatase-inhibitor therapy.

Study design

Phase III, double-blinded, randomized, placebo-controlled study of taselisib plus fulvestrant versus placebo plus fulvestant

Intervention

One group receives taselisib, 4 mg tablet once daily plus fulvestrant im every 28 days.
The other group receives placebo tablet, once daily plus fulvestrant im every 28 days.

Study burden and risks

3 questionnaires (QLQ-32. QLQ-C30, EQ-5D)
Patient diary
Physical examination every cycle
Fasting before a number of blood draws

Most common adverse events: diahrrea, nausea, hyperglycemia, fatigue, stomatitis, decreased appetite, rash and vomitting.

Randomisation risk: the treatment that the patient receives may prove to be less effective or to have more side effects than the other study treatment

Possible risks and discomfort associated with drawing blood: May cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach or fainting when their blood is drawn.

Contacts

Public
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL
Scientific
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

- Postmenopausal women with histologically or cytologically confirmed locally advanced or metastatic estrogen-receptor positive (ER+) breast cancer;- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1;- Endocrine therapy (e.g., fulvestrant) is recommended and treatment with cytotoxic chemotherapy is not indicated at time of entry into the study;- Radiologic/objective evidence of recurrence or progression to the most recent systemic therapy for breast cancer;- Recurrence or progression during or after aromatase inhibitor;- Evaluable or measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1;- Consent to provide tumor tissue (block or a minimum of 20 slides) from the most recent tumor tissue for PIK3CA-mutation testing; a valid cobas PIK3CA mutation result by central testing is required;- Adequate hematologic and end-organ function within 28 days prior to treatment initiation

Exclusion criteria

- HER2-positive disease by local laboratory testing (immunohistochemistry [IHC] 3+ staining or in situ hybridization positive);- Prior treatment with fulvestrant;- Prior treatment with a PI3K inhibitor, mTOR inhibitor (e.g. everolimus), or AKT inhibitor;- Prior anti-cancer therapy within 2 weeks prior to Day 1 of Cycle 1;- Prior radiation therapy within 2 weeks prior to Day 1 of Cycle 1;- All acute treatment-related toxicity must have resolved to Grade </= 1 or be deemed stable by the Investigator;- Prior treatment with > 1 cytotoxic chemotherapy regimen for metastatic breast cancer;- Concurrent hormone replacement therapy;- Known untreated or active central nervous system (CNS) metastases;- Type 1 or Type 2 diabetes mellitus requiring anti-hyperglycemic medications;- History of inflammatory bowel disease or active bowel inflammation;- Clinically significant cardiac or pulmonary dysfunction;- Clinically significant history of liver disease, including cirrhosis, current alcohol abuse, or current known active infection with HIV, hepatitis B virus or C

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2015
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Taselisib
Generic name:	nvt

Ethics review

Approved WMO Date:	18-02-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2015
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-03-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-05-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	19-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-003185-25-NL
ClinicalTrials.gov	NCT02340221
CCMO	NL51145.056.14