A randomized, multicenter, double-blind phase 3 study of amcenestrant (SAR439859) plus palbociclib versus letrozole plus palbociclib for the treatment of patients with ER (+), HER2 (-) breast cancer who have not received prior systemic anti-cancer treatment for advanced disease

Published: 08-09-2020
Last updated: 17-01-2025

The primary objective of this study is to determine whether SAR439859 in combination with palbociclib improves progression free survival (PFS) compared to letrozole in combination with palbociclib in patients with ER +, HER2-advanced breast cancer...

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

Summary

ID

NL-OMON55315

Source
ToetsingOnline

Brief title
EFC15935/AMEERA-5

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Advanced Breast cancer. Metastatic Breastcancer

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Advanced Breastcancer, double-blind, ER+/ Her-, phase 3

Outcome measures

Primary outcome

Progression Free survival

Progression-free survival is defined as the time interval from the date of

randomization to the date

of first documented tumor progression as per Response Evaluation Criteria in

Solid Tumors

(RECIST 1.1) or death (due to any cause), whichever come first.

Secondary outcome

Secondairy endpoints are the overall survival rate, objective response rate,

duration of response,clinical benefit rate, progression-free survival on next

line of therapy (PFS2), PK plasma concentrations, number of participants with

treatment emergent adverse events and SAEs, time to first chemotherapy, and

questionnaires EQ5D-5L, QlQ-C30,QlQ-BR45, QLQ-BR23

Study description

Background summary

The standard first-line treatment has been endocrine therapy (ET) for decades. Recently, targeted therapy, such as a CDK4 / 6 inhibitor, has been combined with primary and secondary-line ET in metastatic breast cancer. These combinations were evaluated in multiple studies with an AI or fulvestrant. Hormone therapy is the basis of any estrogen receptor positive (ER +), human epidermal growth factor receptor 2 negative (HER2-), advanced or metastatic breast cancer treatment, regardless of the treatment line.
SERDs are competitive ER antagonists that also elicit conformational changes in the ER that lead to the degradation of ER. This unique dual action of SERDs can enable blocking of ER signaling. While fulvestrant has served as an important proof-of-concept for the SERD approach, this treatment has been limited by its poor pharmaceutical properties, necessitating intramuscular administration and limiting the dosage, exposure and receptor involvement with limited clinical benefit to consequence.
SAR439859 is a potent, orally bioavailable and selective ERα inhibitor belonging to the SERD class of compounds. SAR439859 antagonizes estradiol binding to ER, but also promotes ERα transition to an inactive conformation leading to receptor degradation up to 98%. SAR439859 may be a new therapeutic option with a better benefit / risk ratio than already approved endocrine monotherapies, such as aromatase inhibitors, tamoxifen and fulvestrant.

Study objective

The primary objective of this study is to determine whether SAR439859 in combination with palbociclib improves progression free survival (PFS) compared to letrozole in combination with palbociclib in patients with ER +, HER2-advanced breast cancer who have no prior systemic anti-cancer therapies for advanced disease. have received.

Study design

A randomized, multicentre, double-blind double-dummy phase 3 study

Intervention

Arm A: SAR439859 + letrozole corresponding placebo + palbociclib,
Arm B: SAR439859-corresponding placebo + letrozole + palbociclib

SAR439859, letrozole and the corresponding placebos are taken orally once daily for a 28 day course

Palbociclib is taken orally on days 1 to 21 for a course of 28 days

Study burden and risks

The risks are related to blood draws, CT or bone scan (radiation burden), biopsy and possible side effects of the study medication.

Contacts

Public
Genzyme Europe BV

Paasheuvelweg 25
Amsterdam 1105BP
NL
Scientific
Genzyme Europe BV

Paasheuvelweg 25
Amsterdam 1105BP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Adult participants with loco-regional recurrent or metastatic disease not amenable to curative treatment

-Confirmed diagnosis of ER+/HER2- breast cancer
-No prior systemic treatment for loco-regional recurrent or metastatic disease
-Measurable disease ie, at least one measurable lesion evaluable per Evaluation Criterion in Solid Tumors (RECIST) v.1.1, or non-measurable bone only disease
-Eastern Cooperative Oncology Group (ECOG) performance status 0-2.
-Participants should be willing to provide tumor tissue
-Capable of giving informed consent

Exclusion criteria

-Known active brain metastases
-Prior neo (adjuvant) treatment with any selective estrogen receptor degrader (SERD)
-Inadequate organ and marrow function
-Disease recurrence while on, or within 12 months of completion of (neo)adjuvant aromatase inhibitor-containing therapy
-Pregnant, breastfeeding, or woman of child bearing potential unwilling to use recommended contraception methods
-Male participants who disagree to follow contraception
-Participants with advanced, symptomatic visceral spread, that are at risk of life-threatening complications in the short term
-Participants with significant concomitant illness

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Completed

Start date (anticipated):	12-02-2021
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Femara
Generic name:	Letrozole
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ibrance
Generic name:	Palbociclib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	n/a
Generic name:	Amcenestrant
Product type:	Medicine
Brand name:	zoladex
Generic name:	gosereline
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-09-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-11-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-02-2021

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-03-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-09-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-10-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-10-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-08-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC 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	EUCTR2020-001824-33-NL
CCMO	NL74493.068.20

Study results

Date completed: 16-08-2022

Results posted: 14-11-2023

Summary results
Trial ended prematurely

First publication
08-12-2022