A Phase III Randomized, Placebo-Controlled Trial of Carboplatin and Paclitaxel with or without the PARP Inhibitor Veliparib (ABT-888) in Her-2 Negative Metastatic or Locally Advanced Unresectable BRCA-Associated Breast Cancer

Published: 10-07-2014
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The primary endpoint is to assess the progression-free survival (PFS) of veliparib in combination with carboplatin (C) and paclitaxel (P) compared to placebo with C/P in subjects with a BRCA1 and/or BRCA2 Mutation and HER2-Negative Metastatic or...

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

Summary

ID

NL-OMON44514

Source
ToetsingOnline

Brief title
M12-914

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
mamma carinoma, metastatic breast cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BRCA-associated, HER-2 negative breast cancer, PARP, Veliparib

Outcome measures

Primary outcome

Progression Free Survival

Secondary outcome

- Overall Survival

- Clinical Benefit Rate

- Objective Response Rate

- Progression Free Survival second-line therapy

- Duration of Overall Response

Study description

Background summary

Breast cancer (BC) is diagnosed in over 1.3 million women worldwide each year and accounts for over 500,000 deaths, making it the leading cause of cancer-related death in women. Although the number of agents approved for the treatment of advanced breast cancer continues to increase, overall survival has changed relatively little and median survival remains unchanged, in the range of 2 to 3 years from initial diagnosis of metastatic disease.

The therapeutic potential of PARP inhibitors was suggested by two clinical trials evaluating PARP inhibition in breast cancer and one clinical trial in ovarian cancer. Therapeutic potential in breast cancer has also been observed

with veliparib in combination with carboplatin + paclitaxel.

This is the first randomized, Phase 3 study of veliparib in HER2-negative metastatic or locally advanced unresectable breast cancer in patients with clinically significant (suspected deleterious or deleterious) germline mutation of BRCA1 or BRCA2.

Study objective

The primary endpoint is to assess the progression-free survival (PFS) of veliparib in combination with carboplatin (C) and paclitaxel (P) compared to placebo with C/P in subjects with a BRCA1 and/or BRCA2 Mutation and HER2-Negative Metastatic or Locally Advanced Unresectable Breast Cancer.

The secondary objectives of the study are to assess overall survival (OS), clinical benefit rate (CBR), objective response rate (ORR), PFS2 and duration of overall response (DOR) in subjects treated with veliparib in combination with C/P versus subjects treated with placebo with C/P. The tertiary objectives are to assess change in ECOG performance status, change in Quality of Life (QoL).

Study design

This is a Phase 3 randomized, double-blind, multinational, multicenter study. Subject randomization will be stratified by estrogen receptor (ER) and/or progesterone receptor (PgR) positive versus ER/PgR negative, prior platinum therapy (yes versus no), and CNS metastases (yes versus no). Subjects will be randomized in a 2:1 ratio to one of the two treatment arms.

This study will be conducted in approximately 200 research sites and approximately 500 subjects will be enrolled.

Intervention

The Screening procedures will be performed within 28 days prior to the first dose of study drug (C1 D-2). Subjects in the veliparib/placebo + carboplatin + paclitaxel treatment arms, have study visits conducted at Day -2, Day 1, Day 8, and Day 15 of Cycle 1 and Day 1, Day 8 and Day 15 of every cycle thereafter (cycle is 21 days). Subject moving to the crossover treatment arm, have study visits conducted at Day 1 and Day 15 of Cycle 1 and Day 1 of every cycle thereafter.

Subjects will continue dosing until they meet the defined discontinuation criteria. When a subject meets the criteria for study discontinuation, a Final Visit will be conducted. All subjects will have one Follow-up Visit approximately 30 days after the last dose of study medication.

Survival information will be collected at two-monthly intervals, beginning on the date the subject is registered off study and until the endpoint of death, until the subject has become lost to follow-up or until study termination by AbbVie.

Study burden and risks

The burden for the subject consist of extra visits to the site, three times an ECG, additional blood draws besides the standard safety labs. Next to this the subject will complete at a maximum 4 questionnaires per visit. Progression of disease will be measured every nine weeks.

The duration of the study will be different for each subject.. Subjects will continue the treatment until progression of disease criteria are met or the subject does not tolerate the treatment.

Based on research the most frequent adverse events are for veliparib in combination with carboplatin and paclitaxel (> 10%): hair loss, joint pains and shortness of breath or difficulty breathing.

Based on research the most frequent adverse events are for veliparib alone (> 10%): Feeling sick to your stomach, feeling tired, decreased red blood cells or hemoglobin (the part of blood that carries oxygen to your body), vomiting, decreased white blood cells; decreased lymphocytes and decreased neutrophils (blood cells that help fight infections), diarrhea, decreased platelets (blood cells which help clot blood and prevent bleeding), decreased appetite, headache, constipation, stomach pain, difficulty falling asleep and/or staying asleep, feeling dizzy, change in the sense of taste and dehydration.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Men and women >= 18 years of age;
- Histologically or cytologically confirmed breast cancer that is either locally advanced or metastatic;
- Locally advanced breast cancer must not be amenable to surgical resection or radiation with curative intent;
- Suspected deleterious or deleterious BRCA1 and/or BRCA2 germline mutation;
- Measurable or non-measurable (but radiologically evaluable) disease per RECIST version 1.1 on computed tomography (CT) scan.

Exclusion criteria

- Received anticancer agent(s) or an investigational agent within 21days prior to C1D-2 or radiotherapy within 28 days prior to C1D-2;
- More than 2 prior lines of cytotoxic chemotherapy (e.g., gemcitabine, doxorubicin, capecitabine) for metastatic disease;
- More than one prior line of platinum therapy for breast cancer;
- Subjects who have progressed on platinum therapy or recurred within 12 months of platinum therapy will be excluded;
- Prior therapy with PARP inhibitors;
- Prior taxane therapy administered for the treatment of metastatic breast cancer with exceptions (see protocol);
- Subjects with active brain metastases or leptomeningeal disease.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-02-2015
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo
Product type:	Medicine
Brand name:	Veliparib
Generic name:	Veliparib

Ethics review

Approved WMO Date:	10-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-11-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	26-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	10-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-09-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	07-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2014-000345-70-NL
ClinicalTrials.gov	NCT02163694
CCMO	NL48835.078.14

Study results

Date completed: 14-02-2023

Summary results
Trial ended prematurely