A Randomized, Phase 2 Study of the Efficacy and Tolerability of Veliparib in Combination with Temozolomide or Veliparib in Combination with Carboplatin and Paclitaxel Versus Placebo Plus Carboplatin and Paclitaxel in Subjects with BRCA1 or BRCA2 Mutation and Metastatic Breast Cancer

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

Summary

ID

NL-OMON40393

Source
ToetsingOnline

Brief title
M12-895

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
mamma carcinoma, metastatic breast cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BRCA1 and 2 mutation carrier, Metastatic breast cancer, PARP, veliparib

Outcome measures

Primary outcome

Progression Free Survival [Time Frame: Radiographic evaluation every 9 weeks,

clinical evaluation every cycle]

Secondary outcome

•Overall Survival [Time Frame: From Randomization until patient's death or 3

years post discontinuation]

•Clinical Benefit Rate (CBR) [Time Frame: From Randomization until patient's

death or 3 years post discontinuation]

•Objective Response Rate [Time Frame: From Randomization until patient's death

or 3 years post discontinuation]

Study description

Background summary

Breast cancer 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. Despite recent advances in breast cancer treatment, with very few exceptions, metastatic breast cancer remains incurable, and the aim of treatment is to palliate symptoms and prolong the time to progression.

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. A therapeutic potential for veliparib has also been suggested in BRCA1/2-mutated breast cancer, and specifically for the utility of the veliparib + TMZ combination. Therapeutic potential in breast cancer has also been observed with veliparib in combination with carboplatin + paclitaxel. This is the first randomized, Phase 2 study of veliparib in locally recurrent or metastatic breast cancer in patients with deleterious germline mutation of BRCA1 or BRCA2.

Study objective

The primary objective of the study is to assess the progression-free survival (PFS) of oral
veliparib in combination with temozolomide (TMZ) or in combination with carboplatin and paclitaxel compared to placebo plus carboplatin and paclitaxel. The secondary objectives of the study are to assess overall survival (OS), clinical benefit rate (CBR), objective response rate (ORR) in those subjects treated with veliparib in combination with TMZ or treated with veliparib plus carboplatin and paclitaxel versus placebo plus carboplatin and paclitaxel. Chemotherapy-Induced Peripheral Neuropathy (CIPN) will be assessed in those subjects treated with veliparib plus carboplatin and paclitaxel versus placebo plus carboplatin and paclitaxel. The tertiary objectives are to assess Eastern Cooperative Oncology Group (ECOG) performance status and quality of life (QoL) and to assess exploratory correlative endpoints.

Study design

This is a Phase 2, randomized, partially blinded, multinational, multicenter study. Subject randomization will be stratified by estrogen receptor (ER) and/or progesterone receptor (PgR) positive versus ER and PgR negative, prior cytotoxic therapy versus no prior cytotoxic therapy and ECOG 0-1 versus 2. Subjects will be randomized in a 1:1:1 ratio to one of the three treatment arms. This study will be conducted in aproximately 120 research sites. The maximum amount of subjects that will be enrolled are 255.

Intervention

The Screening procedures will be performed within 28 days prior to the first dose of study drug (C1D1). For subjects randomized to the veliparib + TMZ

treatment arm, study visits will be conducted at Day 1, Day 15, and Day 22 for the first two cycles and then Day 1 of every cycle thereafter. For subjects randomized to the veliparib/placebo + carboplatin + paclitaxel treatment arms, study visits will be conducted at Day 1, Day 3, and Day 17 of Cycle 1 and Day 1 and Day 3 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 veliparib + TMZ or veliparib/placebo + carboplatin + paclitaxel.
Survival information will be collected at monthly intervals, beginning on the date the subject is registered off study and for up to three (3) years 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, two times an ECG, additional blood draws besides the standard safety labs. Next to this the subject will complete at a maximum 3 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 temozolomide (>= 10%):
Feeling sick to your stomach, feeling tired, decreased platelets, constipation, vomiting, decreased appetite, decreased neutrophils, diarrhea, headache, cough, back pain, decreased red blood cell counts or hemoglobin, dizziness, difficulty in breathing (shortness of breath), pain in joints, abdominal pain, change in sense of taste, trouble with sleeping.

Based on research the most frequent adverse events are for veliparib in combination with carboplatin and paclitaxel (>= 10%):
decreased neutrophils in the blood, feeling tired, decreased white blood cells, feeling sick to your stomach, changes in the nerves that can cause numbness, tingling, or pain in the hands and feet decrease in platelets, decreased hemoglobin or hematocrit, constipation, hair loss, decreased appetite, vomiting, muscle pains, joint pains, diarrhea, cough, shortness of breath or difficulty breathing, difficulty sleeping, headache, swelling of the feet, pain in the arms or legs, dizziness, abdominal pain.

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

•>= 18 years of age, male and female.
•Histologically or cytologically confirmed breast cancer with evidence of metastatic disease.
•Must have a documented deleterious Breast Cancer Gene BRCA1 or BRCA2 germline mutation.
•If Human Epidermal Growth Factor Receptor (HER2) positive, subjects must have received and progressed on at least one prior standard HER2 directed therapy or the subject must be ineligible to receive anti-HER2 therapy.
•Subject has measurable disease by RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) criteria.
•Eastern Cooperative Oncology Group (ECOG) Performance Score of 0-2.
•Subject must have adequate bone marrow, renal and hepatic function.

•Subject must not be pregnant or plan to conceive a child.

Exclusion criteria

•Received anticancer agent(s), an investigational agent within 21 days prior, or radiotherapy within 28 days prior Cycle 1 Day 1
•More than 2 prior lines of cytotoxic chemotherapy
•Prior therapy with temozolomide, a platinum agent, or a PARP (Poly (ADP-ribose) - Polymerase) inhibitor.
•Prior taxane therapy for metastatic disease
•A history of or evidence of brain metastases or leptomeningeal disease.
•A history of uncontrolled seizure disorder
•Pre-existing neuropathy from any cause in excess of Grade 1
•Known history of allergic reaction to cremophor/paclitaxel
•Clinical significant uncontrolled conditions - active infection, myocardial infarction, stroke, or transient ischemic attack, psychiatric illness/social situations that would limit compliance.
•Pregnant or breastfeeding

Study design

Design

Study phase:	2
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):	11-11-2013
Enrollment:	7
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:	Temodal
Generic name:	Temozolomide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Veliparib
Generic name:	Veliparib

Ethics review

Approved WMO Date:	24-04-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-07-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	09-09-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2014
Application type:	Amendment
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:	18-09-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	13-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-08-2016
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	EUCTR2011-002913-12-NL
ClinicalTrials.gov	NCT01506609
CCMO	NL43591.078.13

Study results

Results posted: 27-08-2021

First publication
01-01-1900