

# Efficacy of cabazitaxel in patients with HER2-negative metastatic breast cancer

<b>Submission date</b> 06/02/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/06/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 17/03/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/trials/A-trial-looking-at-cabazitaxel-for-HER-2-negative-breast-cancer-that-has-spread-to-the-brain>

## Contact information

### Type(s)

Scientific

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## **Additional identifiers**

**Clinical Trials Information System (CTIS)**  
2012-000542-35

**Protocol serial number**  
RDD490

## **Study information**

### **Scientific Title**

Phase II multicentre study assessing the efficacy of Cabazitaxel in Patients with HER2-negative metastatic breast cancer and having unresectable brain metastases (CiPHER)

**Acronym**  
CiPHER

### **Study objectives**

Cabazitaxel is an effective cytotoxic agent that crosses the blood brain barrier and we hope to investigate this attribute in this Phase II study across several UK recruitment centres. Potentially this therapy could afford survival advantage. The primary aim of this study is to assess the feasibility of Cabazitaxel use in breast cancer with brain metastases by determining whether there is evidence for Cabazitaxel increasing 18 week survival from 67% to 81%.

The study will require a maximum of 62 patients. The trial would be terminated for futility if 21 or fewer patients out of the first 31 survive to 18 weeks. Otherwise, the remaining 31 patients will be recruited (unless advised to the contrary by the DMC) and the null hypothesis will be rejected if there are more than 47 survivors at 18 weeks out of the 62 patients.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**  
NRES Committee North West Liverpool Central, 22/05/2013, REC ref: 13/NW/0153

**Study design**  
Single-arm Phase II study

**Primary study design**  
Interventional

**Study type(s)**  
Treatment

**Health condition(s) or problem(s) studied**  
Patients with HER2-negative metastatic breast cancer and having unresectable brain metastases.

## **Interventions**

Patients on this study will receive cabazitaxel chemotherapy treatment and palliative radiotherapy will be deferred until evidence of disease progression. These patients will be monitored clinically and radiologically every three and six weeks respectively. Cabazitaxel 25 mg /m<sup>2</sup> given on day 1 of each treatment cycle, intravenously, for one hour every 21 days.

Diagnostic biopsy of primary tissue, urine samples (baseline and end of treatment) and blood samples (baseline, day 1 of each cycle and at end of treatment) will be collected, processed and stored for future research purposes. This will be with the aim of identifying serum and urinary biomarkers of predictive and prognostic significance. Baseline diagnostic tissues will be used for gene expression profiling and linked with serum and urinary biomarkers and proteomic profiles to identify markers of efficacy, resistance and toxicity.

## **Intervention Type**

Drug

## **Phase**

Phase II

## **Drug/device/biological/vaccine name(s)**

Cabazitaxel

## **Primary outcome(s)**

Overall proportion surviving at 18 weeks from registration

## **Key secondary outcome(s)**

1. Progression-free survival (PFS) defined as the time from registration to the first of one of the following: development of disease progression or death from any cause
2. Overall response for extracranial visceral metastases (ORv) as defined in RECIST 1.0 , recorded from the start of treatment to 18 weeks
3. Overall response for CNS lesions (ORc) defined as a best response of at least PR, recorded from the start of treatment to 18 weeks
4. Acute toxicity (CTCAE v4) after each treatment cycle up to 18 weeks (for the purposes of safety, toxicity will be assessed up until 28 days after the last dose of study treatment)
5. Time to radiotherapy (measured from treatment start date until commencement of radiotherapy)
6. Time to neurological deterioration

## **Completion date**

25/07/2018

## **Eligibility**

### **Key inclusion criteria**

First or second line metastatic HER2 negative\* breast cancer

1. Oligometastatic brain disease that is unsuitable for surgical resection and/or stereotactic radiosurgery
2. Age 18 years or over
3. ECOG performance status 0-2
4. Diagnosis of metastatic HER2-negative breast cancer
5. At least one measurable target lesion (RECIST 1.0) in the brain\*\* (unsuitable for resection)

identified by CT scan or MRI within 21 days of registration.

6. Females of child bearing potential who have a negative pregnancy test prior to study entry
7. Agree to use adequate contraception which they agree to continue for 12 months after the study treatment
8. Ability and capacity to comply with study and follow-up procedure
9. Able to provide written informed consent

\*Patients with ER+ve or ER-ve disease are eligible for the study

\*\* Patients with meningeal disease are eligible provided they fit the other criteria. Extracranial disease is not a requirement of this study.

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

Female

### **Total final enrolment**

19

### **Key exclusion criteria**

1. Received prior radiotherapy/radiosurgery to the brain (radiotherapy may be offered on disease progression)
2. Received >2 lines of chemotherapy for metastatic recurrent disease (adjuvant treatment is permitted) prior to registration
3. Received any chemotherapy after the diagnosis of brain metastases
4. Previous hormone therapy if it will not be discontinued before Cabazitaxel treatment
5. Patients who have received an increasing dose of steroids to control CNS symptoms within 14 days of registration (steroid use is permitted only when patient is stable at a specific dose at the time of screening)
6. Visceral metastases with no recorded brain metastases
7. Pregnancy or lactation
8. Prior surgery, radiation, chemotherapy, or other anti-cancer therapy within 28 days prior to registration
9. Patients with a history of other previous malignancy except treated CIN or non melanomatous skin cancer
10. Grade  $\geq 2$  peripheral motor and/or sensory neuropathy
11. Grade  $\geq 2$  mucositis oral
12. History of severe hypersensitivity reaction ( $\geq$  grade 3) to taxanes
13. History of severe hypersensitivity reaction ( $\geq$  grade 3) to polysorbate 80-containing drugs
14. Other concurrent serious illness or medical conditions which make it undesirable for the patient to enter the trial (including uncontrolled diabetes mellitus)

15. Inadequate organ and bone marrow function as evidenced by:

15.1. Haemoglobin < 9.0 g/dL

15.2. Absolute neutrophil count <  $1.5 \times 10^9/L$

15.3. Platelet count <  $100 \times 10^9/L$

15.4. AST/SGOT and/or ALT/SGPT >  $2.5 \times ULN$

15.5. total bilirubin >  $1.0 \times ULN$

15.6. Serum creatinine >  $1.5 \times ULN$ . If creatinine  $1.0 - 1.5 \times ULN$ , creatinine clearance will be calculated according to CKD-EPI formula and patients with creatinine clearance < 60 mL/min should be excluded

16. Active infection requiring systemic antibiotic or anti fungal medication.

17. Participation in another clinical trial with any investigational drug within 30 days prior to registration

18. Administration of potent inhibitors and inducers of P450 3A4/5 enzymes within 7 days of registration, or planned concurrent administration whilst on study. This excludes steroid treatment which is standard care treatment for patients with brain metastases

19. Concomitant vaccination with live attenuated vaccines

**Date of first enrolment**

01/03/2012

**Date of final enrolment**

05/12/2017

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

The Clatterbridge Cancer Centre NHS Foundation Trust

Wirral

United Kingdom

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## **Sponsor information**

**Organisation**

The Clatterbridge Cancer Centre NHS Foundation Trust (UK)

**ROR**

<https://ror.org/05gcq4j10>

# Funder(s)

## Funder type

Industry

## Funder Name

Sanofi: CABAZ\_L\_5958

## Alternative Name(s)

sanofi-aventis, Sanofi US, Sanofi-Aventis U.S. LLC, Sanofi U.S.

## Funding Body Type

Government organisation

## Funding Body Subtype

For-profit companies (industry)

## Location

United States of America

# Results and Publications

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>	Participant information sheet		28/05/2020	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>		11/11/2025	11/11/2025	No	Yes
<a href="#">Plain English results</a>			17/03/2021	No	Yes