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

Submission date
06/02/2013

Recruitment status
No longer recruiting

Registration date
20/06/2013

Overall study status
Completed

Last Edited
17/03/2021

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 /m2 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 ≥2 peripheral motor and/or sensory neuropathy
11. Grade ≥2 mucositis oral
12. History of severe hypersensitivity reaction (≥grade 3) to taxanes
13. History of severe hypersensitivity reaction (≥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 x 109/L
15.3. Platelet count <100 x 109/L
15.4. AST/SGOT and/or ALT/SGPT >2.5 x ULN
15.5. total bilirubin >1.0 x ULN
15.6. Serum creatinine >1.5 x ULN. If creatinine 1.0 - 1.5 x 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
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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?
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No
Plain English results			17/03/2021	No	Yes