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Capecitabine oral chemotherapy with radium-223 in breast cancer patients with bone metastases (CARBON)

Submission date 17/02/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/02/2016	**Overall study status** Completed	
Last Edited 06/03/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-capecitabine-and-radium-223-for-advanced-breast-cancer-carbon

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-003979-29

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 20654

Study information

Scientific Title
A randomized phase IB/IIA study of CApecitabine plus Radium-223 (Xofigo) in breast cancer patients with BONe metastases (CARBON): an open-label interventional study

Acronym
CARBON

Study objectives
In advanced breast cancer, most patients with bone involvement also have metastases in other organs. Thus, a bone-targeted treatment alone is unlikely to be relevant to the majority of patients. Combination strategies with established systemic breast cancer treatments are needed. This is an open-label study which comprises an initial safety phase to establish the feasibility and safety of combining radium-223 at the licensed dose and to the same maximum recommended total dose, but given on a 6 weekly schedule to enable combination with oral capecitabine administered with the usual two weeks on and one week off treatment schedule. The safety phase, if treatment proves to be safe and feasible, will be followed by a randomised extension phase to further characterise the safety profile and provide preliminary information on efficacy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Fulham Research Ethics Committee, 03/02/2016, ref: 16/LO/0052

Study design
Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Breast Cancer; Disease: Bone, Breast

Interventions
Patients in the initial safety phase will receive capecitabine plus radium-223. Patients in the randomised extension phase will be randomised to receive either oral capecitabine alone or capecitabine plus radium-223 (added 07/03/2016).

Usual hospital stock of capecitabine 500mg and 150mg tablets will be used and supplied as trial specific stock according to standard operating procedures within the treating centre. Patients should swallow capecitabine tablets with water 30 min after a meal twice a day. Standard care should be followed regarding missed and vomited doses

Radium-223 50 kBq/kg b.w (55 kBq/kg after implementation of NIST update) will be administered as a slow i.v. injection 6 times at 6 weekly intervals. This treatment can be administered on an outpatient basis. It will be administered on day 1 of each alternate cycle (cycles 2, 4, 6, 8, 10 and 12). A cycle is 21 days in accordance with the standard administration of capecitabine.

Follow Up Length: 12 month(s)

Intervention Type
Mixed

Primary outcome(s)
As of 07/03/2016:
Initial safety phase
1. Dose limiting toxicities

Randomised extension phase
1. Frequency of CTC grade III-IV toxicities with a focus on diarrhoea as the primary dose limiting toxicity
2. Decrease in uNTX from baseline to end of cycle 5 (approximately 15 weeks post trial entry). For patients who progress prior to the end of cycle 5, the decrease in uNTX from baseline to their end of study treatment visit will be used.

Previous primary outcome measures:
To evaluate the safety and toxicity of the combination of radium-223 and capecitabine

Key secondary outcome(s))
As of 07/03/2016:
1. Safety endpoints
1.1. Adverse events (AEs) and serum biochemistry and haematology abnormalities graded according to the Common Toxicity Criteria for Adverse Events (CTC) version 4.03
1.2. Serious adverse events
1.3. Dose delays and reductions due to toxicity
2. Efficacy endpoints
2.1. Changes from baseline in serum bone turnover markers (B-ALP, uNTX, P1NP, CTX and 1CTP) throughout the study period
2.2. Time to occurrence of 1st symptomatic skeletal event (SSE). This is time from registration / randomisation to 1ST SSE. Patients who do not experience an SSE by the time of final analysis will be censored at the last time known to have not experienced as SSE, study withdrawal, start of new treatment or death
2.3. Time to progression of bone disease based on unequivocal progression of existing bone lesions or appearance of one or more new osteolytic bone lesions. This is time from registration /randomisation to progression in bone. Patients who do not progress in bone by time of final analysis will be censored at the last time known to have not progressed in bone, study withdrawal, start of new treatment or death
2.4. Time to progression of extraskeletal disease. This is time from registration / randomisation to progression in extraskeletal non bony sites. Patients who do not progress outside bone by time of final analysis will be censored at the last time known to have not progressed outside bone, study withdrawal, start of new treatment or death

3. Clinical benefit endpoints
3.1. Pain scores using the Brief Pain Inventory (BPI)
3.2. Quality of life using the EORTC BM-22 bone metastases module

Previous secondary outcome measures:
To evaluate the effect of radium-223 on other bone turnover markers (P1NP, CTX, 1CTP, B-ALP)

Completion date
02/08/2021

Eligibility

Key inclusion criteria
Current inclusion criteria, as of 19/03/2018:
1. Female patients with histological evidence of primary breast cancer
2. Bone metastases (with or without soft tissue, lymph node or visceral metastases; brain metastases allowed if stable and untreated for = 8 weeks)
3. = 2 bone lesions confirmed on imaging (plain radiographs, CT or MRI)
4. Systemic chemotherapy with capecitabine is felt to be appropriate by the treating physician due to recent progression of metastatic disease
5. Received = 2 lines of chemotherapy in the metastatic setting. Prior cytotoxic therapy must have been completed = 28 days prior to initiation of study treatment
6. Patient has been on bone targeted therapy (bisphosphonate or denosumab) for at least 6 weeks prior to start of study treatment and no change to bone targeted therapy is expected during the treatment phase of the study.
7. ECOG performance status 0-2
8. Life expectancy = 6 months
9. Laboratory requirements:
9.1. WBC =3.0 x10 9 /l 3000/mm3
9.2. ANC =1.5 x10 9 /l1500/mm3
9.3. Platelet count =100x109/l
9.4. Haemoglobin =10.0g/dL
9.5. Total bilirubin level =1.5 times ULN in treating institution
9.6. AST and ALT = 3 times ULN in treating institution
9.7. Calculated creatinine clearance or estimated GFR > 50mls/min (Cockcroft and Gault or Wright formula may be used according to local practice)
10. Patient must be willing and able to comply with the protocol, including follow-up visits and investigations and use effective contraception if relevant throughout the study and for at least 6 months after treatment completion
11. Must be fully informed about the study and has signed the informed consent form
12. Age at least 18 years

Previous inclusion criteria:
1. Female patients with histological evidence of primary breast cancer
2. Bone metastases (with or without soft tissue, lymph node or visceral metastases; brain metastases allowed if stable and untreated for = 8 weeks)
3. = 2 bone lesions confirmed on imaging (plain radiographs, CT or MRI)
4. Systemic chemotherapy with capecitabine is felt to be appropriate by the treating physician due to recent progression of metastatic disease
5. Received = 2 lines of chemotherapy in the metastatic setting. Prior cytotoxic therapy must have been completed = 28 days prior to initiation of study treatment

6. Patient has been on bone targeted therapy (bisphosphonate or denosumab) for at least 3 months prior to start of study treatment and no change to bone targeted therapy is expected during the treatment phase of the study
7. ECOG performance status 0-2
8. Life expectancy = 6 months
9. Laboratory requirements:
9.1. WBC =3.0 x10 9 /l 3000/mm3
9.2. ANC =1.5 x10 9 /l1500/mm3
9.3. Platelet count =100x109/l
9.4. Haemoglobin =10.0g/dL
9.5. Total bilirubin level =1.5 times ULN in treating institution
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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
34

Key exclusion criteria
1. Received an investigational drug within 4 weeks prior to the first study treatment
2. Received external beam radiotherapy within 4 weeks prior to the first study treatment
3. Presence of imminent or established spinal cord compression based on clinical findings and/or MRI
4. Presence of other currently active (diagnosis within the last 5 years) malignancy (except treated non-melanoma skin cancer (basal or squamous), carcinoma in situ of cervix and superficial bladder cancers).
5. Patients who have had severe and unexpected reactions to fluoropyrimidine therapy or have been diagnosed with dihydropyrimidine dehydrogenase deficiency
6. Received a blood transfusion or Use of erythropoietin within 4 weeks of study treatment
7. Pregnant or breast-feeding women.
8. Treatment with sorivudine or its chemically related analogues, such as brivudine

9. Treatment with phenytoin or warfarin
10. Patients with any other serious illness or medical condition, such as, but not limited to:
10.1. Any uncontrolled infection
10.2. Clinical heart failure (NYHA Heart Failure Class III or IV)
10.3. Active Crohn’s disease or ulcerative colitis
10.4. Bone marrow myelodysplasia
10.5. Uncontrolled coronary artery disease
10.6. Active peptic ulcers
10.7. Malabsorption
11. Any exclusions as per the Xofigo or Capecitabine SmPC

Date of first enrolment
28/09/2016

Date of final enrolment
20/03/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St James' University Hospital
NHS Trust
The Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Weston Park Hospital
Sheffield Teaching Hospitals NHS FT
Whitham Road
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Manchester Cancer Research Centre
The Christie NHS Foundation Trust
Wilmslow Road

Manchester
United Kingdom
M20 4QL

Study participating centre
Clatterbridge Centre for Oncology NHS Foundation Trust
Clatterbridge Road
Bebington
Wirral
Liverpool
United Kingdom
CH63 4JY

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Trust

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Industry

Funder Name
Bayer HealthCare

Alternative Name(s)
BHC

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Funder Name
Yorkshire Cancer Research

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/06/2022	06/03/2024	Yes	No
Protocol article	protocol	15/01/2020	17/01/2020	Yes	No
Basic results		22/07/2022	22/07/2022	No	No
HRA research summary			26/07/2023	No	No