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CORE Trial

Submission date 19/09/2016	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 02/11/2016	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 16/01/2020	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-stereotactic-body-radiotherapy-for-breast-prostate-non-small-cell-lung-cancer-core

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
NCT02759783

Protocol serial number
31452

Study information

Scientific Title
CORE: A randomized trial of conventional care versus radioablation (stereotactic body radiotherapy) for extracranial oligometastases

Acronym
CORE

Study objectives
The principal aim of the trial is to assess whether the addition of SBRT to standard therapy improves survival outcomes, focusing on common primary tumour sites where oligometastatic disease is encountered.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Central Research Ethics Committee, 09/05/2016, ref: 16/LO/0529

Study design
Randomised; Interventional; Design type: Treatment, Surgery

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Extracranial oligometastases

Interventions
Patients will be randomised between SOC and SBRT + SOC in a 1:1 ratio. Patients will be randomised at different stages of their disease depending on the primary tumour site and in accordance with the inclusion and exclusion criteria. Treatment allocation will use minimisation with balancing factors of primary tumour site (breast, NSCLC, prostate) and centre. In tumour sites where there is felt to be a further important prognostic variable which may affect the primary PFS endpoint, a further stratification will be performed, as outlined below, to ensure the 2 treatment groups are balanced.
Breast – ER+ vs ER-
NSCLC – EGFR+ vs EGFR-
Prostate – endocrine naïve vs castrate resistant

SOC only arm: In the SOC only arm, the choice of SOC treatment is at the discretion of the local oncologist (chemotherapy, biological therapy, endrocrine therapy, surgery, palliative radiotherapy or observation).

SBRT + SCO arm: Patients randomised to SBRT+SOC will receive a dose and fractionation regimen dependent on the metastatic site and proximity to dose limiting organs and normal tissues. The average scheme would be 3 treatments over 5 days but the maximum period of SBRT duration could be 8 treatments over 19 days. After SBRT treatment, the patient will be treated with the SOC treatment at the discretion of the local oncologist.

All patients will be reviewed every 3 months with a clinical examination and tumour markers (where applicable) during years 1 and 2, and 6 monthly thereafter to 5 years. Staging and follow up imaging protocols will be tumour type dependent:

1. Breast: 3 monthly CT scans for years 1 and 2, and 6 monthly thereafter to 5 years.
2. NSCLC: 3 monthly CT scans for years 1 and 2, 6 monthly to year 3, then annually to 5 years.
3. Prostate: CT scans will be performed at 6, 12 and 24 months with imaging triggered by appropriate PSA rises.

All patients will have a toxicity assessment at each clinic visit and patient reported quality of life (QOL) assessment at 3, 6, 12, 18 and 24 months.

Intervention Type
Other

Primary outcome(s)
Progression free survival is measured using RECIST at baseline, 3, 6, 9, 12, 15, 18, 21,24, 30, 36, 42, 48, 54 and 60 months post randomisation.

Key secondary outcome(s))
1. Recruitment rate is defined by the proportion of patients recruited into the trial versus the number of patients required
2. SBRT deliverability is defined by the proportion of patients allocation SBRT who received SBRT and within dosimetric constraints outlined in the protocol versus the number of patients allocated SBRT
3. Overall survival is defined as time from randomisation until the time of death from any cause
4. Local lesion control is assessed using RECIST at baseline, 3, 6, 9, 12, 15, 18, 21,24, 30, 36, 42, 48, 54 and 60 months post randomisation.
5. Clinician reported acute and late radiation related toxicity is measured using CTCAE version 4 and RTOG at baseline, end of treatment, 3, 6, 9, 12, 15, 18, 21,24, 30, 36, 42, 48, 54 and 60 months post randomisation
6. Patient reported quality of life is measured using the EORTC QLQ C30 and EQ-5D questionnaires at baseline, end of treatment, 3, 6, 9, 12, 18 and 24 months post randomisation

Completion date
01/10/2019

Eligibility

Key inclusion criteria
1. Age ≥ 18 years
2. WHO performance status 0-2
3. Histological confirmation of primary malignancy (histological confirmation of metastasis is not mandatory but should be performed in any situation where there is diagnostic uncertainty). Patients with breast, NSCLC or prostate primary malignancies are eligible.
4. Predicted life expectancy > 6 months
5. ≤ 3 metastatic lesions (total). A maximum of 2 different organ systems (e.g. liver, lung, bone, nodal) may contain metastases but the total number of lesions must not exceed 3. For example, a patient with 3 liver metastases or 1 liver metastasis and 2 lung metastases would be eligible. A patient with 1 lung metastasis, 1 liver metastasis and an adrenal metastasis is ineligible.

6. All metastases must be visible, imaging defined targets and be suitable for treatment with SBRT in accordance with the dose fractionation options specified in the protocol. (See the associated CORE trial radiotherapy delivery guidelines for detailed SBRT guidance by metastatic site
7. Patients who have received prior ablative therapy (e.g. surgery, RFA or SBRT) for metastatic disease are eligible, as long as this site is controlled on imaging at the point of trial entry and the total number of metastases over time since diagnosis of metastatic disease does not exceed 3. Patients with 2 or 3 metastases in which ablative therapy (e.g. surgery/RFA) to 1 site is deemed appropriate as part of standard therapy may be entered into the trial after ablative treatment, following successful delivery of clinical treatment.
8. Metachronous metastatic disease presentation only. Primary site must be controlled. Disease-free interval from completion of radical treatment (including any adjuvant therapy) to diagnosis of metastases:
8.1. Breast: ≥ 6 months. Patients who have relapsed whilst on adjuvant endocrine therapy are eligible.
8.2. NSCLC: ≥ 4 months
8.3. Prostate: ≥ 6 months. Patients who have relapsed whilst on adjuvant endocrine therapy are eligible
9. Systemic therapy naïve in the metastatic setting
10. Adequate baseline organ function to allow SBRT to all relevant targets dependent on location of metastatic subsite for necessary baseline investigations)
11. Negative pregnancy test (for women of childbearing potential)
12. Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
13. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
245

Key exclusion criteria
1. Intra-cranial metastases
2. Malignant pleural effusion
3. Malignant peritoneal disease
4. Any single metastasis >6cm (>5cm for lung metastases)
5. Prior radiotherapy to a site that precludes safe delivery of SBRT
6. Co-morbidities precluding staging or follow up imaging, or precluding procedures required to

facilitate SBRT
7. Loco-regional nodal relapse where surgery or regional field radiotherapy is standard of care. Patients with supraclavicular, axillary and internalmammary nodal relapse from breast cancer are excluded
8. Spinal cord compression
9. Any condition or significant clinical co-morbidities that precludes the safe delivery of SBRT (eg history of clinically significant diffuse interstitial lung disease if SBRT to lung metastases or lesions adjacent to lungs are considered or clinically significant colitis ie ulcerative colitis /Crohn's disease if SBRT to the pelvis or abdomen is considered)
10. Prostate cancer patients previously relapsing on Androgen Deprivation Therapy (ADT) or CAB and receiving abiraterone, enzalutamide or docetaxel are ineligible
11. Patients whose entry to the trial will cause unacceptable clinical delays to their planned management

Date of first enrolment
07/10/2016

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Institute of Cancer Research
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Sponsor information

Organisation
Royal Marsden NHS Foundation Trust

ROR
https://ror.org/0008wzh48

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

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
The datasets generated during and/or analysed during the current study are/will be available upon request from core-icrctsu@icr.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No