Patients randomised to SBRT will receive a dose and fractionation regimen dependent on the metastatic site and proximity to dose limiting organs and normal tissues (Table 1).

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Inclusion/Exclusion criteria

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.

Inclusion Criteria
- Age ≥ 18 years, WHO performance status 0-2
- Histological confirmation of primary breast, NSCLC, or prostate cancer
- Expectancy: ≥ 6 months
- ≤ 3 metastatic lesions (total) in ≤ 2 different organ systems
- No prior ablative therapy
- Prior to randomisation

Exclusion Criteria
- Prior treatment with systemic therapy for metastatic disease
- Patients with a limited burden of oligometastatic disease
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- Any single metastasis >6 cm (≥ 5 cm for lung metastases)
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SBRT Study Treatment

Quality Assurance

Prior to activation, participating centres need to complete radiotherapy (SBRT) and chemotherapy planning, and then undergo an independent external dosimetry audit and submission of a facility questionnaire and process document. Each oncologist taking part in the trial will need to:
- Pre-accrual: Complete Benchmark exercises (outlining and planning).
- During accrual: Complete a prospective review (outlining and planning).
- Outlining cases are completed on an individual clinician/anatomical site basis. Planning cases are completed on a centre/anatomical site basis.

SBRT + SOC group

SBRT dose and fractionation dependent on site

Follow up

Patients reviewed every 3 months with a clinical exam and tumour markers (where applicable), and 6 months thereafter for 5 years. Further staging and follow up imaging protocols will be tumour type dependent.

Treatment allocation will use minimisation with balancing factors of primary tumour site (breast, NSCLC, prostate), and the following dependent on primary site:
- Breast: ER+/PR+ (relapsed post adjuvant therapy) vs all other subgroups.
- NSCLC: into EGFR+ or the remainder.
- Prostate: patients endocrine therapy naïve vs patients already receiving endocrine therapy for biochemically defined relapse.

Trial Design

Primary endpoint is progression free survival (PFS).

Secondary endpoints include:
- Feasibility of recruitment to a randomised trial of SBRT + SOC vs SOC alone.
- Deliverability of SBRT within dosimetric constraints.
- Acute and late toxicity.
- Quality of life.
- Lesion local control rates in those receiving SBRT.
- Freedom from widespread metastatic disease (FFWMD).
- Overall survival.

The study has a phase II screening design (one-sided alpha=0.20; beta=0.20). The control-arm PFS assumes one third of patients are recruited from each primary tumour site with a median PFS of 5 months for NSCLC, 12 months for breast and 18 months for prostate patients. In order to detect a HR of 0.75, equivalent to a reduction in the median cohort PFS from 12 to 16 months, Target accrual is 206 patients. With a small allowance for dropout, a total of 196 patients are required (135 events) for each oncologist taking part in the trial.

Conduct

Andrew Gaya, Maria Hawkins, Anna Kirby, Merina Ahmed, Nicholas Van As, Isabel Syndikus, Kevin Franks, Suneil Jain, Emma Hall, Vincent Khoo on behalf of CORE TCG

Acknowledgments

CORE (CRUK/14/038) is funded by Cancer Research UK and coordinated by Clinical Trials and Statistics Unit at the Institute of Cancer Research. CORE is supported by the NCRI Radiotherapy Trials Quality Assurance Team (RTTOA). CORE is sponsored by Royal Marsden NHS Foundation Trust

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The Royal Marsden
NHS Foundation Trust

The Institute of Cancer Research

CORE – Randomised trial of Conventional care vs Radioablation (stereotactic body radiotherapy (SBRT)) in extracranial oligometastases (CRUK/14/038)

Andrew Gaya, Maria Hawkins, Anna Kirby, Merina Ahmed, Nicholas Van As, Isabel Syndikus, Kevin Franks, Suneil Jain, Emma Hall, Vincent Khoo on behalf of CORE TCG

Background

- The term oligometastases describes the concept of an intermediary state, in which cancer exists as a limited number of metastases at first, before cells acquire the ability to metastasise more widely.
- Successful eradication of disease at an oligometastatic stage may improve survival outcomes, and may even result in cure for some patients[1,2].
- The CORE trial (Conventional care versus Radioablation (Stereotactic body radiotherapy) in Extracranial oligometastases) evaluates the addition of SBRT to standard therapy improves progression free survival outcomes in patients with a limited burden of oligometastic disease.
- The trial is a phase III, multi-centre, non-blinded, parallel group study.

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Outcomes

The aim of the phase II component of CORE is to demonstrate the feasibility of randomised recruitment, deliverability of the study in an international multi-centre setting and the activity of SBRT based on PFS and OS across the three tumour types. If all three aims are achieved, the trial will be amended to roll into parallel tumour-site specific phase III trials.