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A phase III international randomised trial of single versus multiple fractions for re-irradiation of painful bone metastases

Submission date 19/12/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/12/2005	**Overall study status** Completed	
Last Edited 19/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-a-second-course-of-radiotherapy-for-cancer-that-has-spread-to-the-bone

Study website
http://www.ctg.queensu.ca/trials/default.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00080912

Secondary identifying numbers
SC.20 / CKTO 2004-06

Study information

Scientific Title
A phase III international randomised trial of single versus multiple fractions for re-irradiation of painful bone metastases

Acronym
METRET (METastases RETreatment)

Study objectives
Radiotherapy is an established treatment for painful bone metastases. Most patients in the United Kingdom will receive a single dose of 6 to 8 Gy although fractionated schedules are sometimes still employed. Many patients, particularly those with breast, prostate and renal cancer have a good initial response but later have pain recurrence and may be offered further radiotherapy. Additionally, it has been shown that some patients who fail to respond initially may benefit from re-irradiation. There is no data to inform the optimal radiotherapy schedule for retreatment.

The primary objective of this trial is to compare the efficacy of pain relief after re-irradiation with an 8 Gy single fraction or 20 Gy in five (or eight) fractions in a simple pragmatic two-arm randomised trial. Pain will be measured using the Wisconsin Brief Pain Inventory, which will be sent to patients at intervals by the trials centre.

Secondary objectives include determining the overall incidence of pain relief, studying the relationship between pain relief after re-irradiation and response to previous irradiation, as well as determining the characteristics of the group of non-responders (to both the first and second radiation), and the monitoring or acute severe adverse effects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Bone metastases, malignancy

Interventions
ARM one: 8 Gy (single) one fraction
ARM two: 20 Gy (multiple) five or eight fractions (for spine and/or whole pelvis only)

Patients will be stratified by:
1. Their response to initial radiation as per physician's interpretation of patient history at the time of randomization into responders versus non-responders (i.e. patients who did or did not gain pain improvement after initial radiation)
2. Initial fractionation i.e. single 6-8 Gy versus multiple fractions (20-24 Gy/5-6# and 30 Gy/10#)
3. Centre

Intervention Type
Other

Phase
Phase III

Primary outcome measure
To compare pain relief after re-irradiation of symptomatic bone metastases with 8 Gy or 20 Gy

Secondary outcome measures
1. To determine the overall incidence of pain relief in patients undergoing re-irradiation for symptomatic bone metastases
2. To determine the time to pain progression after re-irradiation
3. To assess the relationship between response to initial radiation and pain relief with re-irradiation
4. To determine the changes in functional interference following re-irradiation using the Brief Pain Inventory (and quality of life [QoL] using EORTC QLQ C30 in Canada and the Netherlands)
5. To determine the characteristics of the group of non-responders (to both the initial and re irradiation)
6. To monitor the incidence of acute severe radiation-related side effects
7. To monitor the incidence of in-field pathological fractures and spinal cord compression

Overall study start date
01/04/2005

Completion date
01/04/2007

Eligibility

Key inclusion criteria
1. Patient must be 18 years of age or older at the time of randomisation
2. Patient must have histologically or cytologically proven malignancy
3. Histological diagnosis may be established from needle biopsy, bone marrow biopsy, cytology, or a surgical biopsy or resection
4. All malignant histologies/cytologies are eligible
5. Plain radiographs, radionuclide bone scans, Computed Tomography (CT) scans and/or magnetic resonance imaging confirm the presence of bone metastases corresponding to clinically painful area
6. Patient has a worst pain score of more than or equal to 2/10 as reported using the Brief Pain Inventory
7. There is no plan to make an immediate change in the analgesic regimen
8. Karnofsky Performance Status more than 50 within one week prior to randomisation
9. The interval between the last fraction of the initial radiation and the date of randomisation in this study is more than four weeks
10. Initial radiation treatment field is reproducible for re-irradiation
11. Pain is arising from the previously irradiated metastasis(es) and not from progressive disease in the adjoining or remote areas
12. Site of pain considered for palliative radiotherapy must be encompassed by the same or smaller treatment field/portal as initial treatment
13. Canada and The Netherlands only:
13.1. Patient is able (i.e. sufficiently fluent) and willing to complete the quality of life questionnaire in English, French or Dutch. The baseline assessment must already have been completed
13.2. Inability (illiteracy in English, French or Dutch, loss of sight, or other equivalent reason) to complete the questionnaires will not make the patient ineligible for the study. However, ability but unwillingness to complete the questionnaires will make the patient ineligible
14. Patient consent must be obtained according to local Institutional and/or University Human Experimentation Committee requirements. It will be the responsibility of the local participating investigators to obtain the necessary local clearance, and to indicate in writing to the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) Study Coordinator that such clearance has been obtained, before the trial can commence in that centre. Because of differing requirements, a standard consent form for the trial will not be provided. A copy of the initial full board Research Ethics Board (REB) approval and approved consent form must be sent to the central office:
14.1. The patient must sign the consent form prior to randomisation or registration
14.2. The consent form for this study must contain a statement which gives permission for the NCIC CTG and monitoring agencies to review patient records
15. Patients must be accessible for treatment and follow-up. Investigators must assure themselves that the patients randomised on this trial will be available for complete documentation of the treatment, adverse events, and follow-up.
16. In accordance with NCIC CTG policy, treatment must begin within four weeks of randomisation

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
850

Key exclusion criteria
1. Clinical or radiological evidence of spinal cord compression at the time of assessment for this study
2. Clinical or radiological evidence of pathological fractures of extremities in the area to be re-irradiated
3. Radiological evidence of high-risk lesions for pathological fractures in the extremities (lytic lesions more than 3 cm or more than 50% cortical erosion of bone diameter) and candidate for surgical intervention. Patients who are NOT surgical candidates are eligible for this study.
4. The treatment area has received prior palliative surgery
5. There is planned surgical intervention on the treated bone
6. Treatment field of initial radiation volume has to be enlarged/modified to accommodate symptomatic disease not previously irradiated, or to provide adequate treatment margin
7. Systemic radiotherapy (Sr-89) has been received within 30 days prior to randomisation
8. Patient has received half body irradiation including the current re-irradiation field within 30 days prior to randomisation

Date of first enrolment
01/04/2005

Date of final enrolment
01/04/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
Radiotherapy Institute Friesland (RIF)
Leeuwarden
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8934 AD

Sponsor information

Organisation

Radiotherapy Institute Friesland (RIF) (The Netherlands)

Sponsor details
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Sponsor type
Not defined

ROR
https://ror.org/05f7htr55

Funder(s)

Funder type
Research organisation

Funder Name
Trans-Tasman Radiation Oncology Group (TROG) (Australia/New Zealand)

Funder Name
Commissie voor Klinisch Toegepast Onderzoek (CKTO) (Netherlands)

Funder Name
National Cancer Institute of Canada (NCIC) (Canada)

Funder Name
Radiation Therapy Oncology Group (RTOG) (USA)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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				No	No
Plain English results				No	Yes
Results article	results	01/02/2014		Yes	No
Other publications	quality of life analysis	01/04/2018		Yes	No