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Pregabalin bone trial

Submission date 18/04/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 24/04/2008	**Overall study status** Completed	
Last Edited 16/06/2016	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-pregabalin-and-radiotherapy-for-pain-caused-by-secondary-cancer-in-the-bones

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PBT 2007-3/10

Study information

Scientific Title
Double-blind randomised controlled trial of pregabalin versus placebo in conjunction with palliative radiotherapy for malignant bone pain

Study objectives
Although cancer-induced bone pain (CIBP) can be very difficult to treat, we are now in the fortunate position of understanding more about its pathophysiology because of the new animal model of CIBP. It is now possible to employ a rat model of CIBP to investigate the underlying neuronal responses. Electrophysiological studies reveal that animals with this pain state have a significantly more excitable spinal cord compared to control animals.

While evidence points to a unique pain state distinct from neuropathic or inflammatory pain, there is a state of ongoing central sensitisation with major changes at the level of the spinal cord. Work from animal models indicates that glutamate is one of the key neurotransmitters involved. There is considerable evidence for involvement of the ionotropic glutamate receptor, the N-methyl D-aspartate (NMDA) receptor. We have treated malignant bone pain in the clinic with ketamine, an NMDA receptor antagonist, with encouraging results. Unfortunately, side effects can limit use of this drug. Additionally, there is increasing evidence that other glutamate receptor subtypes may have significant roles in sensitised pain states (such as metabotropic glutamate receptors). These are not blocked by ketamine or other NMDA receptor antagonists. Agents that have presynaptic activity to reduce glutamate release may be more effective as the net overall effect of glutamate will be reduced to a greater extent than with receptor specific agents. We are interested in the pre-clinical data which seems to support a role for gabapentin in malignant bone pain.

There is clearly a clinical and scientific need to establish if pregabalin can improve on the analgesic effect of radiotherapy alone. This double-blind randomised placebo controlled trial of radiotherapy and pregabalin and best standard care for CIBP is intended to answer this question.

On 15/02/2011 the overall trial end date was changed from 31/10/2010 to 31/05/2011.
On 08/05/2012 the overall trial end date was changed from 31/05/2011 to 30/04/2012.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Multi-centre Research Ethics Committee (MREC), 16/08/2007, ref: 07/MRE00/59

Study design
Double-blind randomised placebo-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 metastasis

Interventions
This study will be a double-blind randomised controlled trial. Patients who are due to receive palliative radiotherapy to cancer induced bone pain will be assessed, if agreeable, for inclusion in the study. The study will be divided into two stages:

Stage 1: run in -
This will last until the patient starts radiotherapy treatment. During the "run-in" period the opioid analgesic regimen in particular will be optimised to ensure optimum analgesia with minimal side-effects - using a defined schedule. The "run-in" period will last days to approximately 2 weeks, depending on the waiting time for palliative radiotherapy. At the point of receiving radiotherapy, patients who have a bone pain score of greater than or equal to 4 on a 0 - 10 Visual Analogue Scale (VAS) will be invited to take part in the next stage of the study, the "assessment phase".

Stage 2: assessment -
It is at this point that randomisation to receive active drug or placebo will take place. This will be day 1 of the titration of the study drug. Patients will be randomised to receive either pregabalin or placebo twice a day, approximately 12 hours apart. Patients will complete dose titration as per a predetermined protocol, with dose increases after each week in the study to reach a maximum dose by the beginning of week 4.

The "assessment" period is from day 1 of the drug (baseline) to 4 weeks after first fraction of radiotherapy (trial endpoint). Treatment and follow-up will continue for 4 weeks after first fraction of radiotherapy. Study treatment dose titration will stop if effective analgesia or side-effects occur.

Discontinuation of study medication:
Due to the slight risk of adverse effects occurring with abrupt withdrawal of pregabalin (dizziness and somnolence), at study endpoint, patients will be instructed to reduce pregabalin gradually over one week. Patients will be advised to decrease dose by 50% every 48 hours to a dose of 75 mg daily and should continue at this dose until the end of the one-week period.

Intervention Type
Mixed

Primary outcome measure
To establish if radiotherapy and pregabalin gives superior analgesia in CIBP than radiotherapy alone.

Primary and secondary outcomes will be measured at study baseline (date of first fraction of radiotherapy) and study endpoint (four weeks from study baseline).

Secondary outcome measures
1. Background, spontaneous and movement-related pain
2. Total opioid requirements, i.e. background and breakthrough doses
3. Tolerability of pregabalin
4. Global quality of life scores (European Quality of Life [EuroQoL] thermometer)
5. Hospital Anxiety and Depression (HAD) scores
6. Changes in sensory responses as assessed by Quantitative Sensory Testing (QST). Modified short version for those patients who want to complete this (20 minutes).
7. Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) only to be done in conjunction with QST
8. Opioid side-effects
9. Withdrawal from study
10. Serious adverse events - pregabalin

Primary and secondary outcomes will be measured at study baseline (date of first fraction of radiotherapy) and study endpoint (four weeks from study baseline).

Overall study start date
01/11/2007

Completion date
30/04/2012

Eligibility

Key inclusion criteria
1. Clearly identifiable bone pain
2. Index bone pain greater than or equal to 4/10
3. Written informed consent
4. Aged greater than or equal to 18 years, either sex
5. Able to complete necessary assessments required as part of the trial
6. Life expectancy greater than two months
7. Due to receive palliative radiotherapy for bone pain

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
206

Key exclusion criteria

1. Aged less than 18 years
2. Current gabapentin/pregabalin use
3. Significant renal impairment (plasma creatinine greater than 1.5 mg/ml, creatinine clearance less than 60 mmls/hr)
4. Change in any tumoricidal therapy before entering the study which may be expected to have an analgesic benefit during the study period
5. Patients receiving bisphosphonates purely as an analgesic regimen which may be expected to have effects during the study period (patients on regular bisphosphonates pre-occurrence of current bone pain allowed)
6. Bed-bound patients
7. Patients who are having palliative radiotherapy to vertebral metastases
8. Patients receiving wide-field irradiation

Date of first enrolment
15/01/2008

Date of final enrolment
30/04/2012

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Edinburgh Cancer Research Centre (CRUK)
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
http://www.nhslothian.scot.nhs.uk/default.asp

Organisation
University of Edinburgh (UK)

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Old College, South Bridge
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United Kingdom
EH8 9YL

Sponsor type
University/education

Website
http://www.ed.ac.uk/

Organisation
NHS Lothian

Sponsor details

Sponsor type
Not defined

Website
http://www.nhslothian.scot.nhs.uk/Pages/default.aspx

ROR
https://ror.org/03q82t418

Funder(s)

Funder type
Charity

Funder Name

Cancer Research UK (CRUK) (UK) - Clinical Trials Advisory and Awards Committee (CTAAC) (ref: C17598/A7250)

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

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?
Results article	results	20/02/2016		Yes	No