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Examining the effect of intravenous zoledronic acid on pleural fluid production, breathlessness and quality of life in patients with a malignant pleural effusion

Submission date
29/09/2011

Recruitment status
No longer recruiting

Registration date
29/09/2011

Overall study status
Completed

Last Edited
22/09/2015

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The pleura are the two thin membranes around the lungs. Cancer can spread to the pleura or originate there, and may be associated with fluid accumulation called a 'malignant pleural effusion'. This compresses the lungs, causes breathlessness and coughing, and shortens the patient's life expectancy. We commonly manage this problem by inserting a tube called a chest drain to remove the fluid. We can also try to stick the linings of the lung together to take away the space into which fluid can accumulate - this is called 'pleurodesis'. A small permanent drain can also be placed to allow the patient to go home and have fluid drawn off when they are breathless. These three options do not address the underlying problem of the cancer cells causing the excessive fluid production. A drug that reduces fluid production may help patients for whom drainage and pleurodesis are inappropriate or have proved unsuccessful, and may allow us to target malignant pleural effusions early and avoid these invasive procedures. Zoledronic acid is a drug that is in common use for patients with cancer that has spread to their bones, for bone thinning (osteoporosis) in women following the menopause, and to treat high calcium levels and some other bone disorders. It is given as a drip and can be given as a one off dose or repeatedly at 3-4 weekly intervals. It has effects on cancer cells and particularly their ability to make new blood vessels. It has been shown to reduce the relapse rate in women with breast cancer when added to other usual treatment. Zoledronic acid reduces the growth of two kinds of cancer of the lung lining and also appears to reduce pleural fluid production in mice. The aim of this study is to find out whether the effect seen in mice translates to humans. This study seeks to examine whether zoledronic acid at its currently used dose reduces the progression of pleural tumours and the accumulation of pleural fluid, and therefore improves symptoms in patients with malignant pleural disease.

Who can participate?
Patients aged over 18 with cancer and a malignant pleural effusion.

What does the study involve?
Participants are randomly allocated to be treated with either zoledronic acid or a placebo (dummy) drug.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
Southmead Hospital (UK).

When is the study starting and how long is it expected to run for?
August 2010 to June 2013.

Who is funding the study?
Novartis Pharmaceuticals UK Limited (UK).

Who is the main contact?
Dr Amelia Dunscombe
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2009-009134-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
8877

Study information

Scientific Title
A double blind randomised controlled trial examining the effect of intravenous zoledronic acid on pleural fluid production, breathlessness and quality of life in patients with a malignant pleural effusion

Study objectives
Malignant pleural disease is common clinical problem, with effusions occurring in 15% of patients diagnosed with cancer during the course of their disease. They indicate a particularly poor prognosis.

Malignant pleural effusions are associated with dyspnoea and recurrent hospital attendances and have a detrimental impact on the quality of life of cancer patients.The most commonly employed management strategy of thoracocentesis and talc pleurodesis has suboptimal success rates and patients frequently undergo repeated invasive procedures as a result. These strategies seek to drain pleural fluid and attempt to obliterate the pleural space but do not target the principle problem of excess fluid accumulation. A drug that reduces pleural fluid production would have the potential to improve symptoms in patients with malignant effusions and might have particular utility in the treatment of patients with 'trapped lung' or severe underlying lung disease for whom pleurodesis is relatively contraindicated or indeed for patients with small effusions at presentation where optimum timing of pleurodesis is controversial.There is a wealth of in vitro and in vivo animal and human evidence to suggest that the amino-bisphosphonate, zoledronic acid (already in common clinical use for skeletal indications) has potent anti-angiogenic and anti-tumour effects. Zoledronic acid has been shown to inhibit growth of mesothelioma cells in mice and reduce pleural fluid accumulation in a maurine model of pleural adenocarcinoma. The addition of ZA to endocrine therapy in breast cancer has recently been associated with highly significant improvements in disease free and relapse free survival.

This pilot study seeks to inform a large multicentre randomised controlled trial examining the effect of zoledronic acid on pleural tumour progression, pleural fluid accumulation, breathlessness and quality of life as compared to placebo in patients with symptomatic malignant pleural effusions and/or thickening

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West 2 REC, 18/5/2009, ref: 09/H0206/12

Study design
Randomised; Interventional; Design type: Treatment

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
Topic: National Cancer Research Network; Subtopic: Lung Cancer; Disease: Lung (small cell), Lung (non-small cell)

Interventions
Intervention arm = zoledronic acid; control arm = placebo

Zoledronic acid, 4g IV: 2 doses as 21 day intervals; Follow Up Length: 2 month(s); Study Entry : Single Randomisation only

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Zoledronic acid

Primary outcome measure
Change in gadolinium uptake and washout rate on Dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI); Timepoint(s): 42 days

Secondary outcome measures
Change in dyspnoea Visula Analogue Scale (VAS) score; Timepoint(s): 42 days

Overall study start date
02/08/2010

Completion date
30/06/2013

Eligibility

Key inclusion criteria
1. Malignant pleural thickening with or without pleural effusion with
1.1. Malignant fluid cytology or
1.2. Malignant pleural biopsy histology or
1.3. In the context of clinically proven cancer elsewhere with no alternative cause found for the

pleural thickening or effusion
2. Age > 18 years; Target Gender: Male & Female ; Lower Age Limit 18 no age limit or unit specified

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30; Description: Pilot study to inform power calculation of a multicentre trial

Key exclusion criteria
1. Chemical or surgical pleurodesis in the preceding 30 days
2. Intravenous (IV) bisphosphonate within the past 3 months or ongoing therapy
3. Ongoing dental disease requiring intervention
4. Significant renal failure (calculated creatinine clearance of < 40ml/min)
5. Hypocalcaemia at randomisation
6. Inability to give informed consent
7. Pregnancy or lactation
8. Known allergy to bisphosphonates or exipients in the intervention preparation
9. Life expectancy < 4 months
10. Current or planned chemotherapy (However patients receiving the oral chemotherapy agent, tarceva who have been on it for more than 3 months can be included)
11. Hormone manipulation therapy initiated in the month before trial entry (however patients receiving long term hormone manipulation can be included)
12. Haematological malignancy
13. Age < 18 years (no upper age limit)
14/. Severe visual impairment.

Date of first enrolment
02/08/2010

Date of final enrolment
30/06/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Southmead Hospital
Bristol
United Kingdom
BS10 5NB

Sponsor information

Organisation
North Bristol NHS Trust (UK)

Sponsor details
Dept of Anaesthesia
Southmead Hospital
Southmead Road Westbury-On-Trym
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals UK Limited

Alternative Name(s)
Novartis UK, NOVARTIS UK LIMITED

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

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	17/03/2015		Yes	No
HRA research summary			28/06/2023	No	No