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Does Adjuvant Zoledronic acid redUce REcurrence in patients with high risk localised breast cancer?

Submission date 20/08/2003	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/08/2003	**Overall study status** Completed	
Last Edited 29/10/2021	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00072020

Secondary identifying numbers
N/A

Study information

Scientific Title
-

Acronym
AZURE

Study objectives
Adjuvant treatment with 4mg zoledronic acid plus chemotherapy and/or endocrine therapy is superior to chemotherapy and/or endocrine therapy alone in improving the disease-free and bone metastasis-free survival of women with breast cancer at high risk of relapse.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands Research Ethics Committee (ref: 03/7/029)

Protocol Version 1.1, dated April 2003 - 19/05/2003;
Protocol Version 1.2, dated June 2003 - 31/07/2003;
Protocol Version 2, dated December 2003 - 08/01/2004;
Protocol Version 3, dated February 2004 - 24/02/2004;
Protocol Version 4, dated July 2005 - 23/07/2005;
Protocol Version 5, dated September 2007 - 08/10/2007;
Protocol Version 6, dated August 2008 - 24/09/2008;
Protocol Version 7, dated August 2010 - 26/08/2010

All other centres will seek ethics approval before recruitment of the first participant.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Patients are randomised to receive either (neo)adjuvant chemotherapy and/or endocrine therapy alone, or (neo)adjuvant chemotherapy and/or hormonal therapy plus zoledronic acid.

The AZURE trial reached target recruitment and therefore closed to recruitment on 20th Jan 2006.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
To determine whether zoledronic acid with chemotherapy and/or endocrine therapy is superior to chemotherapy and/or endocrine therapy alone in improving disease-free survival

Secondary outcome measures
To determine whether zoledronic acid with chemotherapy and/or endocrine therapy is superior to chemotherapy and/or endocrine therapy alone in terms of:
1. Invasive disease-free survival (Added 05/05/2011)
2. Time to bone metastases as first recurrence
3. Time to bone metastases per se
4. Time to distant metastases
5. Overall survival
6. Reducing skeletal-related events* prior to development of bone metastases
7. Reducing skeletal-related events* following development of bone metastases
Additional secondary objectives are:
1. To assess the safety and toxicity of zoledronic acid in this clinical setting
2. To evaluate the influence of prognostic factors, such as estrogen receptor (ER)/progesterone receptor (PR) status, tumour, node, metastasis (TNM) stage, tumour grade, human epidermal growth factor receptor 2 (HER2/neu) (if available) and menopausal status on treatment outcome
3. To use proteomics, tissue micro-array and other modern techniques to identify more specific prognostic indicators for the development of bone metastases and factors that are able to predict specific benefit from bisphosphonate treatment (to be investigated via sub-studies)
* Defined as: fractures, spinal cord compression, radiation therapy to bone, surgery to bone and hypercalcaemia

Overall study start date
01/09/2003

Completion date
30/09/2006

Eligibility

Key inclusion criteria

Patients with stage II or III primary breast cancer

1. Female patients with Stage II/III primary breast cancer, with T stage ≥T1

2. Patients should be receiving/scheduled to receive chemotherapy and/or endocrine therapy

3. Patients receiving neo-adjuvant therapy
a. Must have tumour size of >5 cm (T3), features of locally advanced disease (T4) or biopsy-proven lymph node involvement

b. Should be scheduled to proceed to definitive surgery$ and/or radical radiotherapy with curative intent within 6 months of starting neoadjuvant therapy

c. Time between commencement of neoadjuvant treatment and planned start date of study drug should be ≤30 days

4. Patients receiving adjuvant therapy

a. Must have undergone complete primary tumour resection and treatment of the axillary lymph nodes*, without any prior neoadjuvant therapy#

b. Must have evidence of lymph node involvement

c. Time between definitive surgery and planned start date of study drug should be ≤60 days

5. Performance status: Karnofsky Index ≥80% or Eastern Cooperative Oncology Group (ECOG) 0 and 1

6. Women of childbearing potential must be using a reliable and appropriate method of contraception

7. Age ≥18 years

8. Patient must have given written informed consent prior to any study-specific procedures
$Final definitive surgery is considered to include re-operation for inadequate margins or another bona fide oncological indication
*Patients whose treatment plan is to proceed to further primary tumour resection and/or treatment of the axillary lymph nodes (e.g. clearance or radiotherapy) with curative intent after completion of chemotherapy would be eligible but this must be completed within 9 months of randomisation
#Pre-operative endocrine therapy of less than 30 days would not be classed as prior neoadjuvant therapy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Added 05/05/2011: target 3300 (3352 at time of registration), recruited 3360

Total final enrolment
3360

Key exclusion criteria
1. Metastatic or recurrent breast cancer or a history of breast cancer (aside from ductal carcinoma in situ [DCIS] or lobular carcinoma in situ [LCIS]) prior to the currently diagnosed case
2. History of prior cancers within the preceding 5 years (including previous contralateral breast cancer), aside from non-melanomatous skin cancer or carcinoma in situ of the uterine cervix treated with curative intent
3. History of diseases with influence on bone metabolism, such as Pagets disease of bone, primary hyperparathyroidism or osteoporosis requiring treatment at the time of study entry or considered likely to become necessary within the subsequent 6 months
4. Severe physical or psychological concomitant diseases that might impair compliance with the provisions of the study protocol
5. Prior treatment with bisphosphonates within the past year
6. Serum creatinine >1.5 x Upper Limit of Normal
7. Known hypersensitivity to bisphosphonates
8. Current active dental problems including dental abscess or infection of the jawbone (maxilla or mandible), or a current or prior diagnosis of osteonecrosis of the jaw (ONJ)
9. Recent (within 4 weeks of study entry) or planned dental or jaw surgery (e.g. extractions, implants). Recent dental fillings, teeth scaling and polishing or minor gingival surgery do not exclude the patient.
10. Pregnancy or breast-feeding
11. Use of other investigational drugs in the 30 days prior to study entry. (Patients may be receiving treatments within a clinical trial providing the treatment under test has a licensed indication within your country).

Date of first enrolment
01/09/2003

Date of final enrolment
30/09/2006

Locations

Countries of recruitment
Australia

England

Ireland

Portugal

Spain

Taiwan

Thailand

United Kingdom

Study participating centre
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Sponsor information

Organisation
The University of Sheffield (UK)

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Sponsor type
University/education

ROR
https://ror.org/05krs5044

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals, USA

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

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	safety and tolerability results	01/06/2011		Yes	No
Results article	results	13/10/2011		Yes	No
Results article	ten-year follow-up results	04/05/2021	25/05/2021	Yes	No
Plain English results		19/08/2014	29/10/2021	No	Yes