ISRCTN15749696 https://doi.org/10.1186/ISRCTN15749696

Does zoledronic acid alter levels of reproductive hormones and how does this affect the tumour and bone in pre- and post-menopausal women with early breast cancer?

Submission date
04/09/2017

Recruitment status
No longer recruiting

Registration date
03/10/2017

Overall study status
Completed

Last Edited
30/01/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-zoledronic-acid-for-early-breast-cancer-zolmeno-study

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-005713-67

IRAS number
197918

ClinicalTrials.gov number

Secondary identifying numbers
CPMS 34845

Study information

Scientific Title
The role of ZOLedronic acid and MENOpausal status on the tumour and bone microenvironment in patients with early breast cancer: a single centre, randomised, proof of concept clinical study

Acronym
ZOLMENO

Study objectives
The aim of this study is to identify the mechanisms responsible for the differential effect of zoledronic acid seen in pre- and post-menopausal women with early breast cancer. This study has arisen directly from the AZURE trial which was the first to demonstrate that menopausal status is a significant modifier of the effects of zoledronic acid (ZOL) in early breast cancer in that women who were post-menopausal significantly benefitted from adjuvant ZOL (with prevention of one death in every six), whereas this effect was not seen in pre-menopausal women. It is hypothesised that this differential effect may be linked to differential levels of follistatin and activin in pre- and post-menopausal women.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire & The Humber - Leeds East Research Ethics Committee, 09/06/2016, ref: 16/YH/0151

Study design
Randomized; Both; Design type: Treatment, Drug, Validation of outcome measures

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 to request a patient information sheet Contact: Erica Wallis, Erica.wallis@sth.nhs.uk

Health condition(s) or problem(s) studied

Breast Cancer

Interventions
Participants in both arms receive a single intravenous infusion of zoledronic acid 4mg in 100ml 0.9% sodium chloride over 15 minutes on either day seven pre-surgery or day 21 post-surgery. The purpose of the randomisation is to allow the effect of zoledronic acid to be separated from the effect of surgery and to permit both pre-administration and post administration bone marrow biopsies to be collected whilst the participants are under anaesthetic during surgery. Participants are randomised by the Informatics Team at the Cancer Clinical Trials Office at Weston Park Hospital using a computer generated randomisation schedule which includes age group stratification: 40-54 years and ≥55 years.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Change in serum follistatin measured by ELISA using validated lab kits at day 28 post-ZOL administration.

Secondary outcome measures
The following secondary outcome measures, all compared relative to menopausal status (pre- vs. post-menopausal) and timing of ZOL administration (Group A vs. Group B), includes:
1. Change in serum follistatin measured by ELISA using validated lab kits at day 7 and 28 post-ZOL infusion
2. Change in serum activin measured by ELISA using validated lab kits at day 7 and day 28 post-ZOL infusion
3. Change in serum follistatin measured by ELISA using validated lab kits from day 0 (surgery) to day 21 and day 28 post-surgery
4. Change in serum activin measured by ELISA using validated lab kits from day 0 (surgery) to day 21 and day 28 post-surgery
5. Follistatin and activin levels measured by ELISA using validated lab kits in tumour samples obtained at surgery

Overall study start date
21/09/2015

Completion date
10/12/2024

Eligibility

Key inclusion criteria
1. Female patients aged ≥40 years
2. Histologically confirmed early breast cancer
3. Tumour size more than 1 cm (≥ T1)
4. Any nodal status including unknown (≥N0)
5. Scheduled for surgery as primary treatment

6. Any tumour hormone receptor (ER/PR) or HER2 status
7. ECOG performance status of 0, 1 or 2 (appendix 2)
8. Menopausal status defined clinically by menstrual and clinical history, or where this is indeterminate patient is willing to have biochemical profile testing following consent
9. Measured or calculated Glomerular Filtration Rate (GFR) ≥30 ml/min (Cockcroft and Gault formula, appendix 3)
10. Serum corrected calcium ≥2.2mmol/L
11. APTT 30.5 seconds
12. PT 13.2 seconds or INR <1.5
13. Platelets 100 x 109/L
14. Or clotting abnormalities which are due to be reversed as part of standard care by the time of bone marrow sampling (e.g. stopping anticoagulants prior to surgery)
15. Potentially fertile women must have a negative pregnancy test within 72 hours prior to randomisation, and not be breast-feeding
16. Potentially fertile women must agree to use effective, medically approved, barrier contraception from the time of consent to 30 days after their zoledronic acid infusion
17. Potential participants must be willing to have the required mandatory samples taken, including bone marrow aspiration and trephine at the time of surgery
18. Potential participants must have the mental capacity to understand the study information, make an informed choice regarding participation and to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
40 Years

Sex
Female

Target number of participants
Planned Sample Size: 80; UK Sample Size: 80

Total final enrolment
19

Key exclusion criteria
1. Any previous diagnosis or treatment of cancer that could confound results and endpoints (allowed situations include non-melanomatous skin cancer or superficial bladder cancer)
2. Patients with an estimated life expectancy of <6 months
3. Any diagnosis of a bone marrow disorder
4. Any previous bisphosphonate treatment
5. Use of hormone replacement therapy (HRT) in the past 30 days or a diagnosis of hormonal imbalance such as polycystic ovarian syndrome
6. Current active dental problems including dental abscess or infection of the jawbone (maxilla or mandible), any open oral wounds or a current or previous diagnosis of osteonecrosis of the jaw
7. Recent (within 4 weeks) or planned dental or jaw surgery (recent dental fillings, scaling,

polishing or minor gingival surgery do not exclude the patient)
8. Any other serious medical or psychiatric condition which in the opinion of the investigator could affect participation in the ZOLMENO study, including dehydration, notable electrolyte disturbances, significant use of nephrotoxic, antiangiogenic or hypocalcaemia inducing drugs or history of significant renal failure, which in the opinion of the screening investigator, would render the patient unsuitable for zoledronic acid or sample collection

Date of first enrolment
01/11/2017

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Weston Park Hospital Cancer Clinical Trials Centre
Sheffield Teaching Hospitals NHS Foundation Trust
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Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

ROR

https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
Yorkshire Cancer Research

Alternative Name(s)
YCR

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trial results are planned to be published in a high-impact peer reviewed scientific journal and by scientific conference presentation. Additional documents are available upon request from Erica Wallis (erica.wallis@sth.nhs.uk).

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No