

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	☒ Prospectively registered ☐ Protocol
Registration date 03/10/2017	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 30/01/2026	Condition category Cancer	☐ Individual participant data

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

Clinical Trials Information System (CTIS)

2015-005713-67

Integrated Research Application System (IRAS)

197918

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

Primary study design

Interventional

Study design

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

Study type(s)

Treatment

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

Primary outcome(s)

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

Key secondary outcome(s)

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

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 ($\geq T1$)
4. Any nodal status including unknown ($\geq N0$)
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 ≥ 2.2 mmol/L
11. APTT 30.5 seconds
12. PT 13.2 seconds or INR < 1.5
13. Platelets $100 \times 10^9/L$
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

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

40 Years

Upper age limit

100 Years

Sex

Female

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

United Kingdom

England

Study participating centre

Weston Park Hospital Cancer Clinical Trials Centre

Sheffield Teaching Hospitals NHS Foundation Trust

Whitham Road

Sheffield

England

S10 2SJ

Sponsor information

Organisation

Sheffield Teaching Hospitals NHS Foundation Trust

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

Individual participant data (IPD) sharing plan

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?
Basic results		30/01/2026	30/01/2026	No	No
HRA research summary			28/06/2023	No	No