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Anastrozole versus placebo in post-menopausal women at increased risk of breast cancer

Submission date 07/01/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 26/04/2005	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 24/04/2025	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-anastrozole-to-prevent-breast-cancer-in-postmenopausal-women

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Additional identifiers

Clinical Trials Information System (CTIS)
2004-003991-12

ClinicalTrials.gov (NCT)
NCT00078832

Protocol serial number
N/A

Study information

Scientific Title
An international multi-centre randomised controlled trial of anastrozole versus placebo in post-menopausal women at increased risk of breast cancer

Acronym
IBIS-II Prevention

Study objectives
Primary hypothesis:
To determine if anastrozole is an effective method of preventing breast cancer in postmenopausal women at increased risk of the disease.

Secondary hypothesis:
1. To examine the role of anastrozole in preventing oestrogen receptor positive breast cancer
2. To examine the rate of breast cancer occurrence after cessation of anastrozole
3. To examine the effect of anastrozole on breast cancer mortality
4. To examine the effect of anastrozole on other cancers, cardiovascular disease, fracture rates, and non-breast cancer deaths
5. To examine tolerability and acceptability of side effects experienced by women on the study

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West MREC (Multi-centre Research Ethics Committee) and local ethics committees (LREC), 16/09/2002

Study design

Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
IBIS-II Prevention is a randomised double blind study investigating the use of anastrozole versus placebo in breast cancer prevention. There are two treatment groups:
Group One: anastrozole
Group Two: placebo
Both the anastrozole and the placebo are tablets that are taken once a day for 5 years.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Anastrozole

Primary outcome(s)
Breast cancer incidence

Key secondary outcome(s))
Current secondary measures as of 23/02/2012:
1. Breast cancer mortality
2. Cardiovascular events
3. Osteoporosis
4. Other relevant side effects

Previous secondary measure:
1. Breast cancer mortality
2. Thromboembolic events
3. Cardiovascular events
4. Osteoporosis
5. Other relevant side effects

Completion date
31/05/2021

Eligibility

Key inclusion criteria

All women must be post-menopausal and between the ages of 40 to 70 years.
Postmenopausal status is defined as meeting one or more of the following criteria:
1. Over the age of 60 years
2. Bilateral oophorectomy
3. Aged 60 years or under with a uterus and amenorrhoea for at least 12 months
4. Aged 60 years or under without a uterus and with Follicle-Stimulating Hormone (FSH) more than 30 IU/L

The entry criteria will be age-dependent to reflect the increasing baseline risk with age.

Aged 45 to 70 years - the entry criteria are based on a relative risk of at least twofold and are similar to IBIS-I. At least one of the following must be satisfied:
1. First degree relative who developed breast cancer at age 50 years or less
2. First degree relative who developed bilateral breast cancer
3. Two or more first or second degree relatives who developed breast or ovarian cancer
4. Nulliparous (or first birth at age 30 years or above) and a first degree relative who developed breast cancer
5. Benign biopsy with proliferative disease and a first degree relative who developed breast cancer
6. Mammographic opacity covering at least 50% of the breast in absence of Hormone Replacement Therapy (HRT) use within the last 3 months

Also aged 60 to 70 years - because of their higher baseline risk, women aged 60 to 70 years can enter the study with a smaller relative risk:
7. First degree relative with breast cancer at any age
8. Age at menopause 55 years or older
9. Nulliparous or age at first birth 30 years or above

Aged 40 to 44 years - who are postmenopausal (usually because of a bilateral oophorectomy) are eligible if they satisfy one or more of the following criteria (approximately fourfold risk or greater):
10. Two or more first or second degree relatives who developed breast or ovarian cancer at age 50 years or less
11. First degree relative with bilateral breast cancer who developed the first breast cancer at age 50 years or less
12. Nulliparous (or first birth at age 30 years or above) and a first degree relative who developed breast cancer at age 40 years or less
13. Benign biopsy with proliferative disease and a first degree relative who developed breast cancer at age 40 years or less

All age groups (40 to 70 years) - women who have had certain breast conditions will also be eligible. These are:
14. Lobular Carcinoma In Situ (LCIS)
15. Atypical ductal or lobular hyperplasia in a benign lesion
16. Ductal Carcinoma In Situ (DCIS), diagnosed within the last six months, and treated by mastectomy. Oestrogen Receptor (ER) or Progesterone Receptor (PgR) status of DCIS must be known, and must be greater than 5% positive cells.
17. Women with a ten year risk greater than 5%, who do not fit into the above categories (risk equivalent). All risk equivalent women must be approved by the Steering Committee Co-Chairman (London IBIS central office). These women must have clearly apparent family history

and/or other risk factors indicating appropriate increased risk of breast cancer for their age. Particularly careful assessment of the risk-benefit for these women should be undertaken before a woman from this group is entered.

All women must have:
1. Had a mammogram taken within the last year and showing no evidence of breast cancer
2. Had a baseline bone mineral density scan within the last 2 years (dual-energy X-ray absorptiometry [DXA] either of hip, lumbar spine, forearm) and spinal X-ray
3. Signed a consent form after receiving full information about the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
40 years

Upper age limit
70 years

Sex
Female

Total final enrolment
3864

Key exclusion criteria
Current exclusion criteria as of 23/02/2012
1. Still having periods
2. Have breast cancer, or have had breast cancer in the past (unless you have had DCIS - see criteria for specific age groups)
3. Have had any other cancer in the last five years (except non-melanoma skin cancer or carcinoma in situ of the cervix or Hodgkin's disease if before the age of 30 and treated with mantle therapy.
4. Have had tamoxifen, raloxifene or other Selective Estrogen Receptor Modulators (SERMs) for more than six months in the past 5 years. (women in IBIS-1 are eligible if they have been off the therapy for more than five years.
5. Want to carry on taking HRT that contains oestrogen
6. Have had (or are planning to have) your breast(s) removed (a mastectomy) to try and prevent breast cancer
7. Have any other serious medical conditions
8. have had treatment with non-approved experimental drugs during the 6 months before randomisation.
9. History of Lactose or gluten intolerance.
10. Life expectancy of less than 10 years or other medical condition which would significantly interfere with the ability to accept the trial treatment.

Previous exclusion criteria
1. Still having periods
2. Have breast cancer, or have had breast cancer in the past (unless you have had DCIS - see criteria for specific age groups)
3. Have had any other cancer in the last five years (except non-melanoma skin cancer or carcinoma in situ of the cervix)
4. Have had tamoxifen, raloxifene or other Selective Estrogen Receptor Modulators (SERMs) for more than three months in the past
5. Have taken part in the IBIS 1 trial
6. Want to carry on taking HRT that contains oestrogen
7. Have had (or are planning to have) your breast(s) removed (a mastectomy) to try and prevent breast cancer
8. Have any other serious medical conditions
9. Have taken any other drug as part of a clinical trial within the last three months

Date of first enrolment
25/05/2003

Date of final enrolment
31/01/2012

Locations

Countries of recruitment
United Kingdom

England

Australia

Belgium

Chile

Denmark

Egypt

Finland

Germany

Hungary

Ireland

Italy

Malta

New Zealand

Pakistan

Peru

Portugal

Russian Federation

Switzerland

Türkiye

Study participating centre
Centre for Cancer Prevention
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Sponsor information

Organisation
Queen Mary University of London (UK)

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK)

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

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?
Results article	cognition substudy results	01/10/2008		Yes	No
Results article	results	22/03/2014		Yes	No
Results article	substudy results	01/12/2014		Yes	No
Results article	adherence results	01/02/2018		Yes	No
Results article	results	03/03/2021	04/03/2021	Yes	No
Results article	long-term results	12/12/2019	06/10/2021	Yes	No
Protocol article	protocol	01/12/2003		Yes	No
Other publications	Results of case control study of IBIS-II participants measuring serum hormone levels	05/12/2023	11/12/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results				No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes