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

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

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

Study website

http://www.ibis-trials.org/

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number 2004-003991-12

IRAS number

ClinicalTrials.gov number NCT00078832

Secondary identifying numbers N/A

Study information

Scientific Title

An international multi-centre randomised controlled trial of anastrozole versus placebo in postmenopausal 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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

No longer available

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 measure

Breast cancer incidence

Secondary outcome measures

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

Overall study start date

25/05/2003

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

Age group

Adult

Lower age limit

40 Years

Upper age limit

70 Years

Sex

Female

Target number of participants

Target: 3500. Final: 3864

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

Australia

Belgium

Chile

Denmark

Egypt

England

Türkiye	
United Kingdom	
Study participating centre	
Centre for Cancer Prevention London	
United Kingdom EC1M 6BQ	
Sponsor information	
Organisation	
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Organisation Queen Mary University of London (UK) Sponsor details	
Organisation Queen Mary University of London (UK)	

Finland

Germany

Hungary

Ireland

Italy

Malta

New Zealand

Pakistan

Portugal

Switzerland

London England

Russian Federation

Peru

United Kingdom E1 2EF +44 (0)20 7882 7275 sponsorsrep@bartshealth.nhs.uk

Sponsor type

University/education

Website

http://www.jrmo.org.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, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The first major analysis was completed in 2013 (https://pubmed.ncbi.nlm.nih.gov/24333009/), a major follow up analysis was published in 2019 (https://pubmed.ncbi.nlm.nih.gov/31839281/). The final analysis for purposes of CSR is to be completed in 2021. Follow up is now conducted via a new long-term follow-up study on a separate protocol (REC 19/LO/0984, IRAS 258590) (study registration pending). The next major follow-up is not due until 2024.

Intention to publish date

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?
Plain English results				No	Yes
<u>Protocol</u> <u>article</u>	protocol	01/12 /2003		Yes	No
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
Other publications	Results of case control study of IBIS-II participants measuring serum hormone levels	05/12 /2023	11/12 /2023	Yes	No