An international study designed to answer reliably whether, for women who have hormone sensitive early breast cancer (the most common type of breast cancer), 10 years of adjuvant tamoxifen (a hormone treatment) confers more benefit than just 5 years in terms of reducing the risk of relapse and improving overall, long-term survival: Adjuvant Tamoxifen - Longer Against Shorter (ATLAS)

Submission date	Recruitment status No longer recruiting	Prospectively registered			
12/10/2012		☐ Protocol			
Registration date	Overall study status	Statistical analysis plan			
18/10/2012	Completed	[X] Results			
Last Edited	Condition category	[] Individual participant data			
29/06/2015	Cancer				

# Plain English summary of protocol

Background and study aims

We know from previous studies of many thousands of women with breast cancer that taking tamoxifen each day, for at least the first few years after surgery, reduces the risk of the breast cancer returning. Tamoxifen does this by interfering with the effect of the natural female hormones on the growth of any traces of breast cancer that may have remained. What is not known, though, is exactly how long women should carry on taking tamoxifen. Most women nowadays receive treatment for about five years, but it might be that 10 years of tamoxifen could be even better. This is why we are doing this study, called ATLAS, to help find out reliably which treatment duration is best in terms of reducing the risk of the breast cancer coming back, and improving long-term survival.

### Who can participate?

Any woman with breast cancer (where the cancer has been removed by surgery) and who has been taking tamoxifen for some time, and where the woman and her doctor are uncertain whether she should keep on taking it for a few more years, or whether she should now stop.

### What does the study involve?

The ATLAS collaboration aims to randomly allocate many thousands of women to one of two

groups: one group stopping tamoxifen after some years of treatment and one group continuing for at least 5 extra years. Several hundred hospitals in many countries world-wide were invited to participate in ATLAS. After discussing the study with her doctor (and family/friends) a woman must sign an information and consent leaflet. Half of the women will be asked to continue taking tamoxifen for at least another five years (unless, later on, new evidence or some reason emerges why they should stop), and the other half will be asked to stop tamoxifen now and to stay off it (unless, later on, new evidence or some reason emerges why they should restart). No special tests or investigations are required to join the study and the woman's own doctor always remains responsible for her wellbeing. There is just a short annual follow-up form which asks for one line of information on the current status of each woman in the study. All information is treated in strict confidence and stored securely at the central study office in Oxford. No individual woman is identified in the study results.

What are the possible benefits and risks of participating?

We very much hope that taking tamoxifen for longer than a few years will provide extra protection against the breast cancer returning and as a result will save many extra lives, and that there will be enough extra benefit to outweigh any side-effects. We know that there is a small risk that tamoxifen will cause cancer of the lining of the womb (endometrium) - which, if caught early, can be successfully treated by hysterectomy. We also know, though, that a few years of tamoxifen has, so far, prevented many more breast cancers coming back than the few womb cancers it has caused. Tamoxifen might also increase the risk of an internal blood clot (thromboembolism), but this may well be counterbalanced by a reduction in the risk of having a heart attack because of the cholesterol-lowering effect of tamoxifen. It is only through studies like ATLAS that we will be able to estimate reliably the balance of benefits and risks of 10 years of tamoxifen compared with just 5 years, so that doctors can then ensure that they give their patients the optimal treatment as well as knowledgeably explaining how the benefits and risks balance out.

### Where is the study run from?

ATLAS is coordinated by the University of Oxford's Clinical Trial Service Unit & Epidemiological Studies Unit, which has a very long history in conducting large international trials like this.

When is the study starting and how long is it expected to run for?

ATLAS started in 1995, completed recruitment of 15 262 women in March 2005, and all women had completed their 5 year trial treatment period by March 2010. Follow-up in ATLAS will continue until 2015 by which time, there should be clear answers on the main question being addressed.

Who is funding the study?

The study has received funding from Cancer Research UK, the UK Medical Research Council, the US Army Breast Cancer Research Program and the EU (Biomed Programme).

Who is the main contact? Dr Christina Davies christina.davies@ctsu.ox.ac.uk

# **Contact information**

**Type(s)**Scientific

#### Contact name

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# Additional identifiers

Clinical Trials Information System (CTIS)

2004-000735-29

ClinicalTrials.gov (NCT)

NCT00003016

Protocol serial number

MHRA CTA: 21584/0002/001; EudraCT number: 2004-000735-29

# Study information

#### Scientific Title

An international randomised trial, involving tens of thousands of women, of 10 versus 5 years of adjuvant tamoxifen in the treatment of oestrogen receptor positive breast cancer, to assess the effects on relapse free and overall survival

#### **Acronym**

**ATLAS** 

### Study objectives

The worldwide randomised evidence now shows that 5 years of adjuvant tamoxifen, following the initial management of early breast cancer, greatly reduces the risk of relapse and improves long-term survival. Tamoxifen is now used by about 1 million women worldwide, avoiding about 20,000 deaths from breast cancer annually. However, there is substantial uncertainty as to whether more than 5 years of hormonal treatment produces even greater benefit. The fundamental aim of ATLAS is to assess reliably the benefits and risks (in terms of recurrence of the disease and long-term survival) of prolonging adjuvant tamoxifen by an extra 5 years in breast cancer patients who have already had about 5 years of treatment.

# Ethics approval required

Old ethics approval format

# Ethics approval(s)

Oxford Tropical Research Ethics Committee, 06/01/2003, ref: 035-02

### Study design

International multicentre randomised controlled trial

### Primary study design

Interventional

### Study type(s)

Screening

### Health condition(s) or problem(s) studied

Operable, oestrogen receptor positive breast cancer already trated with ~5 years of adjuvant tamoxifen

#### **Interventions**

Random allocation was either to stop tamoxifen immediately, using no placebo tablets and restarting endocrine therapy only if a definite indication was thought to have emerged, or to continue tamoxifen for another 5 years (total 10 years), stopping before then, or changing to another endocrine therapy, only if a definite contra-indication was thought to have emerged. The tamoxifen regimen used both before and during the trial treatment period was almost always 20 mg/day oral Nolvadex. (In countries where continuing up to or beyond 5 years was not affordable for many patients, ATLAS supplied free Nolvadex to enable a woman to receive 5 years of tamoxifen prior to enrolment in ATLAS and for the full 5-year post-randomisation period.) All other aspects of patient management were at the doctor's discretion.

### **Intervention Type**

Drug

#### Phase

Not Applicable

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

Tamoxifen

# Primary outcome(s)

- 1. Recurrence (loco-regional, contralateral or distant)
- 2. Breast cancer mortality

# Key secondary outcome(s))

- 1. Overall mortality
- 2. Various first events before recurrence:
- 2.1. Cancer incidence (particularly uterine, including endometrial)
- 2.2. Hospital admissions for particular reasons (particularly uterine or vascular)
- 2.3. Cause-specific mortality

### Completion date

01/12/2015

# **Eligibility**

### Key inclusion criteria

Women were eligible for randomisation if:

- 1. They had had early breast cancer (in which, by definition, all detected disease could be removed surgically)
- 2. They had subsequently been on adjuvant tamoxifen for several years and were still on it (or had stopped only recently, and could therefore resume treatment without much interruption)
- 3. They still appeared clinically free of disease (with any local recurrence removed and no distant recurrence ever detected)
- 4. Long-term follow-up appeared practicable; and, fundamentally,
- 5. Substantial uncertainty was shared by the woman and her doctor about whether to stop tamoxifen or to continue for several more years, so compliance with random allocation to stop or to continue both seemed likely. There were no restrictions on age, type of initial surgery or histology, hormone receptor status, nodal status or what other treatments had also been given.

### Participant type(s)

Patient

# Healthy volunteers allowed

No

### Age group

Adult

#### Sex

Female

### Key exclusion criteria

Any perceived contraindications to continuing tamoxifen precluded entry. These were specified not by the ATLAS protocol but by the judgment of the responsible clinician. However, the protocol suggested as possible contraindications to tamoxifen continuation (and hence to trial entry):

- 1. Intended or actual pregnancy or breast feeding
- 2. Retinopathy
- 3. Need for coagulation therapy
- 4. Significant endometrial hyperplasia
- 5. Any other serious toxicity thought to be due to tamoxifen
- 6. Negligibly low risk of breast cancer death
- 7. Presence of another major life-threatening disease

### Date of first enrolment

01/03/1995

#### Date of final enrolment

01/03/2005

# Locations

#### Countries of recruitment

United Kingdom

Argentina				
Australia				
Belarus				
Belgium				
Brazil				
Chile				
China				
Colombia				
Croatia				
Cuba				
Czech Repul	olic			
Egypt				
Estonia				
France				
Greece				
Hong Kong				
India				
Iran				
Ireland				
Israel				
Italy				
Japan				
Latvia				
Lithuania				
Mexico				

England

South Africa
Spain
Taiwan
Tunisia
Türkiye
United States of America
Study participating centre Clinical Trial Service Unit and Epidemiological Studies Unit Oxford United Kingdom OX3 7LF
Sponsor information

Netherlands

New Zealand

Oman

Paraguay

Poland

Portugal

**ROR** 

Funder(s)

Funder type

Charity

https://ror.org/052gg0110

**Russian Federation** 

#### **Funder Name**

Cancer Research 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** 

#### **Funder Name**

Medical Research Council (UK)

### Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

### **Funding Body Type**

Government organisation

### **Funding Body Subtype**

National government

#### Location

United Kingdom

#### **Funder Name**

AstraZeneca\* (UK)

### Alternative Name(s)

AstraZeneca PLC, Pearl Therapeutics, AZ

### Funding Body Type

Government organisation

### Funding Body Subtype

For-profit companies (industry)

#### Location

United Kingdom

### Funder Name

US Army Breast Cancer Research Program (USA)

### **Funder Name**

EU-Biomed (EU)

### Funder Name

\*AstraZeneca had no involvement in the scientific design or management of ATLAS, which is sponsored by the University of Oxford, the host organisation of the Clinical Trial Service Unit and Epidemiological Studies Unit (the international coordinating centre of ATLAS).

# **Results and Publications**

Individual participant data (IPD) sharing plan

# IPD sharing plan summary

# **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	09/03/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes