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Long-term outcomes and predictive factors for survival in premenopausal breast cancer treated with tamoxifen

Submission date 01/11/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 06/12/2019	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 02/10/2023	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Breast cancer accounts for 1/3 of all malignant diagnosis among females world-wide and is often detected in an early stage. The 5-years survival of breast cancer is about 90%, both due to early screening detection and adjuvant therapy. Despite this, breast cancers might develop recurrence throughout the 20 years after diagnosis. For premenopausal women, breast cancer is a leading cause of death and patients are still being under- and over-treated due to imperfect models to predict outcomes. The possibility to de-escalate therapy, without detrimental effect on survival, is warranted. A majority of breast cancer tumours are sensitive to endocrine treatment, and the patients are generally recommended adjuvant endocrine therapy alone or with additional chemotherapy. Tamoxifen is the most recommended oral drug as adjuvant endocrine therapy in premenopausal women.
This study aims to analyse tissue samples taken during an earlier trial and relate their characteristics to the long-term outcomes in the patients who took part in the earlier trial

Who can participate?
Participants from the earlier SBII:2 trial (1986-1991)

What does the study involve?
Tissue samples collected during the original SBII:2 trial will be analysed and their characteristics compared to the long-term outcomes of the patients

What are the possible benefits and risks of participating?
None

Where is the study run from?
Skåne University Hospital, Sweden

When is the study starting and how long is it expected to run for?
May 2018 to December 2024

Who is funding the study?
Governmental funding for clinical research within the Health Care Sector

Who is the main contact?
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Contact information

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SBII:2 BioLong (1)

Study information

Scientific Title
Premenopausal patients randomized to adjuvant tamoxifen versus not: long-term survival in relation to genomic and tumor related factors

Acronym
SBII:2 BioLong

Study objectives
Comprehensive genomic and histopathological characterization of primary tumours can improve prediction of long-term prognosis and tamoxifen response in premenopausal patients

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 02/02/2017 Lund ethics committee (Box 133, 221 00, Lund; +46 2224180; eva.elvstrand@epn.lu.se), ref: 2015/6
2. Approval for long-term follow-up (Dnr number LU 2015/350) and genomic analyses (Dnr LU 2017/97)

Study design
Prospective-retrospective multicentre interventional randomized trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Premenopausal patients with invasive breast cancer

Interventions
The SBII:2 BioLong study is based on a prospective multicenter randomized clinical trial with > 30 years of follow-up of adjuvant tamoxifen

We will collect formalin-fixed archival tissue for gross evaluation of tumour-infiltrating lymphocytes, characterization of them and assessment of lymphovascular invasion in relation to the primary outcome. RNA and DNA will be extracted to enable RNA profiling by PAM50 and additional gene expression analysis with the 360TM panel. Mutational analysis is scheduled to include ESR1, p53, FGFR and PI3K to identify mutations of importance for tamoxifen resistance. The PAM50 and Risk of Recurrence has been thoroughly evaluated on tumors from postmenopausal patients allocated to hormonal therapy and provides additional prognostic information to conventional prognostic markers. Data on prognosis by PAM50 for premenopausal women is sparse and restricted to less than 10 years of follow up. Surrogate subtyping will additionally be compared to the intrinsic subtypes in terms of prognostic capacity

The original SBII:2 trial (1986-1991) is unique as its inclusion was restricted to premenopausal patients and the control arm includes patients without any systemic therapy, the intervention arm received two years of therapy with tamoxifen. The 30 years of follow-up regarding breast cancer mortality, breast cancer-free interval (BCFi) and distant recurrence-free interval (D-RFi) has been published. The SBII:2 BioLong study will add important genomic and histopathological data to improve our knowledge on factors of importance for long-term prognosis in premenopausal patients.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
BCFi (Breast cancer free interval) over the ~30-year period, measured using patient notes

Secondary outcome measures
1. D-RFi (Distant Recurrence Free interval) over the ~30-year period, measured using patient notes
2. Breast cancer mortality over the ~30-year period, measured using patient notes
3. Overall mortality over the ~30-year period, measured using patient notes

Overall study start date
01/09/2014

Completion date

31/12/2024

Eligibility

Key inclusion criteria
Patients radically operated for invasive breast cancer stage II in the SBII:2 trial

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
500

Total final enrolment
564

Key exclusion criteria
1. Postmenopausal status
2. Metastatic disease

Date of first enrolment
01/05/2018

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Sweden

Study participating centre
Skåne University Hospital
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Sponsor information

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Sponsor type
Government

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ROR
https://ror.org/012a77v79

Funder(s)

Funder type
Government

Funder Name
Governmental funding for clinical research within the Health Care Sector

Funder Name
Fre Bertha Kamprad Foundation

Funder Name
Anna och Edwin Bergers Foundation

Funder Name
Gyllenstiernska Krapperup Foundation

Funder Name

Funder Name
The Clinical Cancer Research Foundation in Jönköping

Results and Publications

Publication and dissemination plan
The SBII:2 BioLong Study will continuously be presented at international congresses and in publications, we anticipate to publish the first report in 2020

Intention to publish date
31/12/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		12/05/2019	06/12/2019	No	No
Interim results article	results on predictive value of tumour-infiltrating lymphocytes	23/12/2020	29/12/2020	Yes	No
Interim results article	PAM50 subtyping and ROR score add long-term prognostic information in premenopausal breast cancer patients	09/05/2022	10/05/2022	Yes	No
Interim results article	Relationship between tamoxifen treatment and breast cancer gene expression	29/09/2023	02/10/2023	Yes	No