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Primary Prevention of Anthracycline-induced Cardiotoxicity with L-Carnitine in patients with breast Cancer (PPACC): pilot study

Submission date 02/04/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 02/04/2007	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 12/02/2019	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00247975

Secondary identifying numbers
MCT-78520

Study information

Scientific Title
Primary Prevention of Anthracycline-induced Cardiotoxicity with L-Carnitine in patients with breast Cancer (PPACC): pilot study

Acronym
PPACC

Study objectives
Primary hypothesis:
Compared to placebo, L-carnitine will reduce the cytotoxic effects of epirubicin on Left Ventricular Ejection Fraction (LVEF).

Secondary hypothesis:
Compared to placebo, patients treated with L-carnitine will have:
1. Smaller increases in LV end-systolic and end-diastolic volumes
2. Lower serum Troponin T (TnT) and Brain Natriuretic Peptide (BNP) levels
3. A reduced incidence of "anthracycline-induced cardiotoxicity"
4. Higher serum L-carnitine levels
5. Similar occurrence of adverse events (breast cancer response, seizures, etc.,)

We will also test the hypothesis that TnT, BNP, serum L-carnitine levels correlate with changes in LVEF, end systolic volume, and end diastolic volume.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the Human Research Ethics Board of University of Ottawa Heart Institute (Canada) on the 7th October 2005 (ref: UOHI 2006-124).

Study design
One centre, two arm, double blind, randomised, parallel group, placebo controlled trial, with study participant, study investigator, caregiver, outcome assessor and data-analyst blinding

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
Experimental group: L-Carnitine therapy plus chemotherapy (FEC-100):
Oral L-carnitine (3 grams daily) for three days prior to chemotherapy, 1 gram of intravenous L-carnitine (5 cc over five minutes, prior to chemotherapy) on the day of chemotherapy and oral L-carnitine (3 grams daily) for three days after chemotherapy.

Control group: placebo (matching L-Carnitine therapy) plus chemotherapy (FEC-100):
Oral placebo for three days prior to chemotherapy, intravenous placebo (5 cc over five minutes, prior to chemotherapy) on the day of chemotherapy and oral placebo for three days after chemotherapy.

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Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
L-Carnitine, 5-fluorouracil, epirubicin, and cyclophosphamide

Primary outcome measure
1. Change in Ejection Fraction (EF) (measure by Radionuclide Angiocardiography [RNA]) at one year, compared to the patient's own baseline. LVEF is used clinically to assess patients' eligibility for continued chemotherapy.

Secondary outcome measures
1. LV end-systolic and end-diastolic volumes (RNA)
2. LV diastolic dysfunction (Echocardiography [ECHO])
3. Serum TnT and BNP measured with each cycle of chemotherapy (immediately prior to and three days after chemotherapy)
4. Composite outcome of: cardiac death, clinical congestive heart failure, reduction in EF requiring termination of anthracycline therapy (LVEF reduction greater than or equal to 10% and LVEF less than 50%), dexrazoxane use or "anthracycline-induced cardiotoxicity"
5. Adverse events (e.g. chemotherapy efficacy, seizures, nausea, diarrhoea)

A secondary analysis of correlation of serum biomarkers (serum L-Carnitine levels, serum TnT, BNP) with surrogate markers of cardiotoxicity (LVEF, LV volumes and diastolic dysfunction) will also be performed.

Overall study start date
01/11/2005

Completion date
31/10/2008

Eligibility

Key inclusion criteria
1. Breast cancer patients (stages I, II, III) eligible for adjuvant epirubicin chemotherapy (5-Fluorouracil, Epirubicin, and Cyclophosphamide [FEC]-100)
2. Eastern Cooperative Oncology Group (ECOG) performance status equals zero to two
3. Informed consent

Amended as of 20/04/2007:
1. Women, aged greater than or equal to 18 years
2. Breast cancer patients (stages I, II, III) eligible for adjuvant epirubicin chemotherapy (FEC100)
3. HER2 negative breast cancer by immunohistochemistry (IHC3+) and/or fluorescent in-situ hybridization
4. Eastern Cooperative Oncology Group (ECOG) performance status equal to zero to two
5. Ability to understand and the willingness to sign a written informed consent document
6. Women of child-bearing potential must agree to use adequate contraception prior to study entry and for the duration of study participation. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately

Participant type(s)
Patient

Age group
Not Specified

Lower age limit
18 Years

Sex
Not Specified

Target number of participants
128 (Amended to 144 as of 20/04/2007)

Key exclusion criteria
1. Resting LVEF less than 50%
2. Previous anthracycline therapy or contraindication to anthracycline
3. Contraindication to L-carnitine therapy
4. Dexrazoxane therapy at the time of enrolment

5. Participation in another randomised clinical trial
6. Significant cardiac disease (previous myocardial infarction, congestive heart failure, haemodynamically significant valvular heart disease)
7. Medication that may affect LV function or symptoms of heart failure (beta-blockers, amiodarone, Angiotensin Converting Enzyme [ACE]-inhibitors, calcium channel blockers, digoxin)
8. Aged less than 18 years or inability to give informed consent
9. Evidence of metastatic breast cancer
10. Patients unable to participate in a study requiring long term follow up
11. Abnormal baseline: Complete blood count (Haemoglobin [Hb] less than 100 mg/L, Platelets [Plt] less than 100 x 10^9/L, White Blood Cells [WBC] less than 4 x 10^9/L), creatinine, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) or bilirubin greater than 1.5 times the upper limit of normal

Amended as of 20/04/2007:
1. Resting LVEF less than 50%
2. Previous anthracycline therapy or contraindication to anthracycline
3. Contraindication to L-carnitine therapy
4. Dexrazoxane therapy at the time of enrollment
5. Participation in another randomised clinical trial
6. Significant cardiac disease (previous myocardial infarction, congestive heart failure, hemodynamically significant valvular heart disease)
7. Medication that may affect LV function or symptoms of heart failure (b-blockers, amiodarone, ACE-inhibitors, calcium channel blockers, digoxin)
8. Pregnant or lactating women
9. Evidence of metastatic breast cancer.
10. Patients unable to participate in a study requiring long term follow up
11. Abnormal baseline: Complete blood count (Hb less than 100 mg/L, Plt less than 100 x 10^9/L, WBC less than 4 x 10^9/L), Creatinine AST, ALT or Bilirubin greater than or equal to 1.5 the upper limit of normal

Date of first enrolment
01/11/2005

Date of final enrolment
31/10/2008

Locations

Countries of recruitment
Canada

Study participating centre
University of Ottawa Heart Institute
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Sponsor information

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University of Ottawa Heart Institute (Institut de cardiologie de l'Université d'Ottawa) (Canada)

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Sponsor type
University/education

Website
http://www.ottawaheart.ca/UOHI/

ROR
https://ror.org/03c4mmv16

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca/ (ref: MCT-78520)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration