

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

ClinicalTrials.gov (NCT)
NCT00247975

Protocol serial number
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).

Primary study design

Interventional

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

Study type(s)

Treatment

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.

Contact for public queries:

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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(s)

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

Key secondary outcome(s)

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.

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

Healthy volunteers allowed

No

Age group

Not Specified

Lower age limit

18 Years

Sex

Not Specified

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 $100 \times 10^9/L$, White Blood Cells [WBC] less than $4 \times 10^9/L$), 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 $100 \times 10^9/L$, WBC less than $4 \times 10^9/L$), 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

Ontario

Canada

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Sponsor information

Organisation

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

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

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Not provided at time of registration