ISRCTN12964275 https://doi.org/10.1186/ISRCTN12964275

Evaluation of the effects of simvastatin in metastatic breast cancer patients

Submission date 24/09/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 11/10/2019	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 02/09/2020	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Preclinical studies support the anticancer activity of statins, however, the existing clinical evidence is inconsistent and not definitive. The aim of this study is to assess the possible cancer chemosensitizing effect of a statin (simvastatin) in metastatic breast cancer (MBC) patients.

Who can participate?
MBC patients undergoing a chemotherapy course of carboplatin and vinorelbine

What does the study involve?
Patients are randomly allocated to receive a 15-day course of either simvastatin or placebo (dummy drug) at day -7 of each chemotherapy cycle. The primary endpoints are objective response rate (ORR) and toxicity, and the secondary endpoint is overall survival (OS).

What are the possible benefits and risks of participating?
Although the beneficial effects of statins in lowering cholesterol are well established, their importance in the area of cancer therapeutics is now gaining greater recognition. At present there is ample evidence to suggest that statins could be used in breast cancer. It provides solid ground for further research on whether statins can improve the efficacy of commonly used cytotoxic agents if given in combination. Possible risks: simvastatin known toxicity.

Where is the study run from?
Al-Baironi Hospital (Syria)

When is the study starting and how long is it expected to run for?
December 2010 to July 2017

Who is funding the study?
Damascus University (Syria)

Who is the main contact?
Prof. Lama Youssef
ylama@hotmail.com

Contact information

Type(s)
Scientific

Contact name
Prof Lama Youssef

Contact details
International University of Science and Technology
Kiwan Land Campus
Damascus
Syria
ylama@hotmail.com
+963-935-797914
ylama@hotmail.com

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Damascus University/15073/

Study information

Scientific Title
Evaluation of the effects of lipophilic statins on the responsiveness of metastatic breast cancer patients to chemotherapy regimens

Study objectives
Preclinical studies support the anticancer activity of statins, however, the existing clinical evidence is inconsistent and not definitive. This study aimed at evaluating a postulated cancer chemosensitizing effect of a statin (simvastatin) in a cohort of metastatic breast cancer (MBC) patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/11/2013, Scientific Research Ethics Committee at the Faculty of Pharmacy, Damascus University (7 Nissan Street, Mazzeh, Damascus, Syria; Tel: +963 (0)112131871), Number: 10

Study design
Prospective single-center randomized double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Metastatic breast cancer

Interventions
Patients were randomly allocated to receive a 15-day course of either simvastatin (40 mg) or placebo at the day -7 of each chemotherapy cycle.

Chemotherapy regimen was conducted every 3 weeks according to the hospital protocol as follows; carboplatin (Carboplatin “Ebewe”), Area under the curve (AUC) 4, intravenously on day 1 and vinorelbine (Navelbine®) intravenously (25 mg/m2) or orally (60 mg/m2) on days 1 and 8 of each cycle. Simvastatin 40 mg or placebo administered orally once daily for 15 days starting at the day -7 of each chemotherapy cycle.

Primary endpoints were objective response rate (ORR) and toxicity, and secondary endpoint was overall survival (OS).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Carboplatin, vinorelbine, simvastatin

Primary outcome measure
1. Objective response rate (ORR) calculated based on both complete response + partial response. Patients’ response classified according to the response evaluation criteria in solid tumor (RECIST) (version 1.1) as follows: complete response (CR): complete disappearance of clinical evidence of disease for a minimum of 8 weeks; partial response (PR): decreased in tumor burden ≥30%; stable disease (SD): decreased by <30% or increased by <20%; progressive disease (PD): increase in tumor burden by ≥20%; and non-evaluable response due to specific reasons (e. g., early death or toxicity). To assess tumor progression, physical examination, tumor markers

(carcinoembryonic antigen (CEA) and cancer antigen 15–3 (CA15-3)), and radiological studies were conducted at baseline and every three cycles, and bone scan was repeated by the end of the sixth cycle
2. Treatment related-toxicity graded according to the Common Terminology Criteria for Adverse Events, version 4 at each cycle

Secondary outcome measures
Overall survival defined as the time from study entry to death from any cause over the follow-up period (the follow-up lasted until death or the cutoff date of July 2017)

Overall study start date
28/12/2010

Completion date
01/07/2017

Eligibility

Key inclusion criteria
1. Female patients attending the breast cancer unit at Al-Baironi Hospital
2. Confirmed diagnosis of metastases (stage IV) prior to commencing chemotherapy course consisting of carboplatin and vinorelbine
3. Age between 20 and 75 years
4. Adequate function of major organs (including cardiac, hepatic and renal functions)
5. ECOG Performance Status score ≤2

Participant type(s)
Patient

Age group
Mixed

Sex
Female

Target number of participants
82

Total final enrolment
82

Key exclusion criteria
1. Pregnant patients
2. Previous treatment with statins or carboplatin and vinorelbine within 30 days of the study

Date of first enrolment
11/08/2011

Date of final enrolment
30/07/2012

Locations

Countries of recruitment
Syria

Study participating centre
Al-Baironi Hospital
Harasta
Damascus
Syria
-

Sponsor information

Organisation
Damascus University

Sponsor details
Baramka
Damascus
Syria
-
+963 (0)11 33923192
info@damascusuniversity.edu.sy

Sponsor type
University/education

Website
http://damascusuniversity.edu.sy

ROR
https://ror.org/03m098d13

Funder(s)

Funder type
University/education

Funder Name
Damascus University

Results and Publications

Publication and dissemination plan
Planned publication after registration is completed.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available upon request from Lama A Youssef, B.Pharm, PhD (ylama@hotmail.com).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	10/08/2020	02/09/2020	Yes	No