

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 ☒ 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
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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Protocol serial number

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

Primary study design

Interventional

Study design

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

Study type(s)

Treatment

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(s)

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 $\geq 30\%$; stable disease (SD): decreased by $<30\%$ or increased by $<20\%$; progressive disease (PD): increase in tumor burden by $\geq 20\%$; 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

Key secondary outcome(s)

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)

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

Healthy volunteers allowed

No

Age group

Mixed

Sex

Female

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

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Sponsor information

Organisation

Damascus University

ROR

<https://ror.org/03m098d13>

Funder(s)**Funder type**

University/education

Funder Name

Damascus University

Results and Publications**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