

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Sep 2026

Comparison of the effect of sacubitril/valsartan with enalapril in the prevention of cardiotoxicity caused by the co-treatment of doxorubicin and trastuzumab in patients with breast cancer: a randomized and controlled clinical trial

Protocol summary

Study aim

Comparison of the effect of sacubitril/valsartan with enalapril in the prevention of cardiotoxicity caused by the co-treatment of doxorubicin and trastuzumab in patients with breast cancer

Design

In one group, patients will receive sacubitril/valsartan at a dose of 50 mg daily for three months. In the parallel group, patients will receive enalapril at a dose of 5 mg daily for three months.

Settings and conduct

Clinical trial - Isfahan University of Medical Sciences

Participants/Inclusion and exclusion criteria

Inclusion Criteria: Adult patients newly diagnosed with HER2-positive breast cancer who have not received any anthracycline-containing chemotherapy regimen in the past. Exclusion Criteria: Patients with a systolic blood pressure less than 100 mmHg. Patients with contraindications for medications from the ACE inhibitor, ARB, and neprilysin inhibitor families. Patients who experience potential adverse effects or allergic reactions to sacubitril/valsartan or enalapril during treatment. Patients who develop another serious illness during the intervention and are required to receive various medications affecting the cardiovascular system.

Intervention groups

Based on which group the patient has been randomly assigned to, a dose of 50 mg daily of sacubitril/valsartan or 5 mg daily of enalapril will be prescribed for the patient for a minimum of three months.

Main outcome variables

Prevention of cardiac toxicity due to the combined treatment of doxorubicin and trastuzumab.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20180722040556N11**

Registration date: **2025-01-20, 1403/11/01**

Registration timing: **prospective**

Last update: **2025-01-20, 1403/11/01**

Update count: **0**

Registration date

2025-01-20, 1403/11/01

Registrant information

Name

Azadeh Moghaddas

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-02-18, 1403/11/30

Expected recruitment end date

2026-03-20, 1404/12/29

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of the effect of sacubitril/valsartan with enalapril in the prevention of cardiotoxicity caused by the co-treatment of doxorubicin and trastuzumab in patients with breast cancer: a randomized and controlled clinical trial

Public title

Comparison of the effect of sacubitril/valsartan with enalapril in the prevention of cardiotoxicity caused by the co-treatment of doxorubicin and trastuzumab in patients with breast cancer: a randomized and controlled clinical trial

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Adult patients newly diagnosed with HER2-positive breast cancer who have not received any anthracycline-containing chemotherapy regimen in the past. These patients are to be treated with an AC regimen containing 60 mg/m² of doxorubicin and 600 mg/m² of cyclophosphamide for 4-6 cycles, followed by treatment with trastuzumab. Patients are expected to receive at least three cycles of trastuzumab (typically 6 mg/kg every three weeks) alone or in combination with or after a taxane-containing regimen if necessary, following the doxorubicin regimen. Study participants must have a baseline left ventricular ejection fraction (EF) of at least 50% (≥50%). They should have no history of cardiovascular diseases such as heart failure, angina, or hypertension. The patient must provide consent to participate in the study and cooperate with the protocol, which includes a monitoring period of at least three months.

Exclusion criteria:

Patients with a systolic blood pressure of less than 100 mmHg. Patients with contraindications to the use of ACE inhibitors, ARBs, and neprilysin inhibitors. Patients who experience potential side effects or allergic reactions to sacubitril/valsartan or enalapril during treatment. Patients with renal failure with a GFR of less than 45 ml/min/1.73 m². Patients with serum potassium levels higher than 5 mmol/L. Patients who have experienced adverse effects such as angioedema or cough from taking enalapril or other ACE inhibitors. Patients who develop another serious illness during the intervention and are required to receive various medications that affect the cardiovascular system.

Age

From 18 years old

Gender

Female

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size

Target sample size: 86

Randomization (investigator's opinion)

Randomized

Randomization description

The randomization of samples will be conducted based on the block randomization method. The sampling method involves entering information such as the number of treatment groups, block sizes (multiples of the number of groups), and the total number of patients into online software designed for this calculation. Based on the codes obtained from the final analysis, the type of medication received by each patient will be determined. In this study, since there are two treatment groups, blocks of 4 (a multiple of 2) will be used. The anticipated sample size of patients will be randomly divided into two groups: those receiving sacubitril/valsartan and those receiving enalapril, using this sampling method. In this way, according to the order of patient enrollment in the study (based on inclusion criteria), each patient will be assigned a code, and then based on the treatment group assigned to that code in the software output, the patient will be placed in one of the treatment groups for sacubitril/valsartan or enalapril.

Blinding (investigator's opinion)

Double blinded

Blinding description

To ensure the blinding of the study, a clinical pharmacy specialist will design random codes using the relevant online software and inform the clinical pharmacy resident which patient, identified by a specific number, will receive which medication. The medications will then be prepared by the research team, and based on the code assigned to each patient, the prescribed medication will be provided for three months at the outset. During this three-month period, since the patient is under the supervision of the oncologist at Seyed Al-Shohada Center, the clinical pharmacy resident will monitor the patient and ensure adherence to the medication protocol according to the research study plan. When patients visit the relevant clinics, they will be screened by the research team. If they qualify for entry into the study, they will receive a code based on the randomization process and will collect their medication from the clinical pharmacy resident. The physician responsible for conducting the baseline and three-month echocardiograms (the study physician) will not have any information about the patient's code or the medication being administered. The echocardiographic images and data will be provided to the analyzing physician without mentioning the received medication, solely assigned with a random code for each patient.

Placebo

Not used

Assignment

Parallel

Other design features

This study is a clinical trial. It is anticipated that sample collection will take place over a two-year period (in the years 2024 and 2025) on hospitalized or outpatient patients at the Cardiovascular Research Institute of Isfahan (affiliated with Isfahan University of Medical

Sciences) and at the Seyed Al-Shohada Hospital clinic.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Isfahan university of medical sciences

Street address

Isfahan University of medical Sciences, Hezar jarib street, Isfahan, Iran

City

Isfahan

Province

Isfahan

Postal code

8174673461

Approval date

2024-11-25, 1403/09/05

Ethics committee reference number

IR.MUI.PHANUT.REC.1403.123

Health conditions studied

1

Description of health condition studied

Breast cancer patients

ICD-10 code

C50

ICD-10 code description

Malignant neoplasm of breast

Primary outcomes

1

Description

The extent of changes in left ventricular systolic function before and after the intervention

Timepoint

Before the intervention began and after three months of taking either enalapril or sacubitril/valsartan.

Method of measurement

Examination of echocardiographic indices including GLS and assessment of cardiac troponin enzyme.

Secondary outcomes

empty

Intervention groups

1

Description

Intervention Group: Patients with HER2-positive breast cancer undergoing AC treatment will receive Sacubitril/Valsartan at a daily dose of 50 mg for a minimum of three months. These patients are at risk of heart failure due to the use of cardiotoxic medications, and the aim of this intervention is to evaluate the impact of this medication on reducing cardiac complications resulting from cancer treatments. After obtaining informed consent and identification by the interventionist, the medication will be administered randomly and without the patient's knowledge to prevent any bias in the results. Throughout the study, compliance with medication intake will be closely monitored, and if less than 80% compliance is observed, the patient will be withdrawn from the study to ensure the validity of the final data. Additionally, side effects and clinical changes in patients will be regularly monitored.

Category

Prevention

2

Description

Control Group: Patients with HER2-positive breast cancer undergoing AC treatment will receive Enalapril at a daily dose of 5 mg for a minimum of three months. This group also consists of patients who are at risk of heart failure due to cardiotoxic medications, and the purpose of administering Enalapril is to compare its effects with those of Sacubitril/Valsartan in reducing cardiac complications. Similar to the intervention group, after obtaining informed consent and identification, the medication will be administered randomly and without the patient's knowledge. Compliance with medication intake will also be closely monitored, and if less than 80% compliance is observed, the patient will be withdrawn from the study. Furthermore, side effects and clinical changes in these patients will also be regularly monitored to determine the actual impact of treatment on their heart health.

Category

Prevention

Recruitment centers

1

Recruitment center

Name of recruitment center

Seyedoshohadda Hospital

Full name of responsible person

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2**Recruitment center****Name of recruitment center**

Isfahan Cardiovascular Research Institute

Full name of responsible person

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Sponsors / Funding sources1**Sponsor****Name of organization / entity**

Esfahan University of Medical Sciences

Full name of responsible person

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Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Esfahan University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin**Type of organization providing the funding**

Academic

Person responsible for general inquiries**Contact****Name of organization / entity**

Esfahan University of Medical Sciences

Full name of responsible person

Azadeh Moghaddas

Position

Associate Professor

Latest degree

Ph.D.

Other areas of specialty/work

Medical Pharmacy

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Person responsible for scientific inquiries**Contact****Name of organization / entity**

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Full name of responsible person

Azadeh Moghaddas

Position

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Latest degree

Ph.D.

Other areas of specialty/work

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Person responsible for updating data**Contact****Name of organization / entity**

Esfahan University of Medical Sciences

Full name of responsible person

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Position

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Latest degree

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Other areas of specialty/work

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

All collected data

When the data will become available and for how long

From May 2026

To whom data/document is available

All academic centers

Under which criteria data/document could be used

All documents with citation

From where data/document is obtainable

Email address

What processes are involved for a request to access data/document

After sending a request, we will call the related person and the data will be revealed in less than one week.

Comments