Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 2026

Evaluation of the Efficacy of Sacubitril/Valsartan Compared with Enalapril in the Prevention of Cardiotoxicity Induced by Taxane and Trastuzumab Therapy in Patients with HERʏ-Positive Breast Cancer: A Randomized Controlled Trial

Protocol summary

Study aim
Comparison of Sacubitril/Valsartan versus Enalapril in the Prevention of Taxane- and Trastuzumab-Induced Cardiotoxicity 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 with newly diagnosed HER2-positive breast cancer who have not previously received any taxane- or trastuzumab-containing chemotherapy regimen. Exclusion Criteria: Patients with systolic blood pressure (SBP) below 100 mmHg. Patients with contraindications to angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or neprilysin inhibitors. Patients who develop potential adverse effects or hypersensitivity reactions to sacubitril/valsartan or enalapril during the treatment period. Patients with renal impairment, defined as an estimated glomerular filtration rate (eGFR) below 45 mL/min/1.73 m². Patients with serum potassium levels above 5 mmol/L. Patients with a history of adverse reactions to enalapril or other ACE inhibitors, including angioedema or cough. Patients who develop another serious medical condition during the intervention period that necessitates treatment with 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 Taxane- and Trastuzumab-Induced Cardiotoxicity

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20180722040556N13**
Registration date: **2026-11-15, 1405/08/24**
Registration timing: **prospective**

Last update: **2026-11-15, 1405/08/24**
Update count: **0**

Registration date
2026-11-15, 1405/08/24

Registrant information

Name
Azadeh Moghaddas

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-11-22, 1405/09/01

Expected recruitment end date
2027-05-22, 1406/03/01

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Evaluation of the Efficacy of Sacubitril/Valsartan Compared with Enalapril in the Prevention of Cardiotoxicity Induced by Taxane and Trastuzumab Therapy in Patients with HERϒ-Positive Breast Cancer: A Randomized Controlled Trial

Public title
Prevention of Cardiotoxicity Induced by Taxane and Trastuzumab Therapy
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
1. Adult patients with newly diagnosed HER2-positive breast cancer who have not previously received any taxane- and trastuzumab-containing chemotherapy regimen. 2. Patients scheduled to receive a taxane-based chemotherapy regimen consisting of either paclitaxel 80 mg/m² IV weekly or docetaxel 75–100 mg/m² IV every three weeks, in combination with trastuzumab (typically 6 mg/kg IV every three weeks). 3. Patients must have a baseline left ventricular ejection fraction (LVEF) of ≥ 50% at study enrollment 4. Patients must have no history of cardiovascular diseases, including heart failure, angina, or hypertension. 5. Patients must provide informed consent to participate in the study and agree to comply with the study protocol, including a minimum follow-up period of three months.
Exclusion criteria:
1. Patients with a systolic blood pressure of less than 100 mmHg. 2. Patients with contraindications to angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), or neprilysin inhibitors. 3. Patients who develop potential adverse effects or hypersensitivity reactions to sacubitril/valsartan or enalapril during the course of treatment. 4. Patients with renal impairment, defined as an estimated glomerular filtration rate (eGFR) of less than 45 mL/min/1.73 m². 5. Patients with a serum potassium level greater than 5 mmol/L. 6. Patients who have experienced adverse effects, such as angioedema or cough, following the use of enalapril or other ACEIs. 7. Patients who develop another serious medical condition during the intervention period that necessitates treatment with medications affecting the cardiovascular system.
Age
From **18 years** old
Gender
Female

Phase
3
Groups that have been masked

- Participant
- Care provider
- Outcome assessor
- Data and Safety Monitoring Board

Sample size
Target sample size: **86**
Randomization (investigator's opinion)
Randomized
Randomization description
Sample randomization will be performed using the block randomization method. The randomization process involves entering information such as the number of treatment groups, block size (a multiple of the number of treatment groups), and total sample size into an online randomization tool [1]. Based on the allocation codes generated by the software, the treatment assignment for each patient will be determined. In this study, since there are two treatment groups, blocks of four (a multiple of two) will be used. The anticipated sample of eligible patients will be randomly allocated to one of two groups: the sacubitril/valsartan group or the enalapril group. Specifically, patients will be assigned a unique identification code in the order in which they are enrolled in the study, provided they meet the inclusion criteria. Each patient will then be allocated to either the sacubitril/valsartan or enalapril treatment group according to the allocation sequence generated by the randomization software for the corresponding code.
Blinding (investigator's opinion)
Double blinded
Blinding description
To ensure blinding of the study, the clinical pharmacy specialist will generate the randomization codes using the designated online software and inform the clinical pharmacy assistant which medication should be dispensed to each patient according to their assigned code. The study medications will then be prepared by the research team, and each patient will receive a three-month supply of the assigned medication at the beginning of the study, based on their allocated code. Throughout the three-month study period, patients will remain under the supervision of the oncologist at Seyed Al-Shohada Hospital. The clinical pharmacy assistant will monitor the patients to ensure adherence to the prescribed medication regimen in accordance with the study protocol. Patients attending the relevant clinics will be screened by the research team for eligibility. Those who meet the inclusion criteria will be assigned a code according to the randomization sequence and will receive their medication from the clinical pharmacy assistant. The physician responsible for performing baseline and three-month follow-up echocardiography (the study physician) will remain blinded to both the patients' assigned codes and the medications they receive. Echocardiographic images and data will be provided to the echocardiography analyst without any information regarding the medication received by the patient. Each patient's echocardiographic records will be identified solely by a randomly assigned code to maintain blinding during image analysis.
Placebo
Not used
Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Isfahan University of Medical Sciences

Street address
Faculty of Pharmacy, Isfahan University of medical Sciences, Hezar jarib street, Isfahan, Iran

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Isfahan

Province
Isfehan

Postal code
81746-73461

Approval date
2026-10-14, 1405/07/22

Ethics committee reference number
IR.MUI.PHANUT.REC.1405.101

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: The intervention will involve identifying patients with HER2-positive breast cancer who are scheduled to receive a taxane-containing chemotherapy regimen consisting of either paclitaxel (80 mg/m² IV weekly) or docetaxel (75–100 mg/m² IV every three weeks), in combination with trastuzumab (typically 6 mg/kg every three weeks). Eligible patients will have no pre-existing heart failure but will be at increased risk of developing heart failure due to exposure to potentially cardiotoxic anticancer therapies. Patients will be identified by the investigator, and informed consent will be obtained prior to enrollment.Patients will receive sacubitril/valsartan at a dose of 50 mg daily for a minimum of three months. The primary objective of this intervention is to evaluate the potential cardioprotective effects of sacubitril/valsartan in reducing cardiac complications associated with cancer treatment.Following patient identification and obtaining written informed consent, treatment allocation will be performed randomly, and patients will be blinded to their assigned treatment to minimize potential bias in the study outcomes. Medication adherence will be carefully assessed throughout the study. Patients with medication adherence below 80% will be withdrawn from the study to ensure the validity and reliability of the final data. Furthermore, adverse events and clinical changes will be regularly monitored throughout the study period.

Category
Prevention

2

Description
Control group: Patients with HER2-positive breast cancer who are scheduled to receive a taxane-containing chemotherapy regimen consisting of either paclitaxel (80 mg/m² IV weekly) or docetaxel (75–100 mg/m² IV every three weeks), in combination with trastuzumab (typically 6 mg/kg every three weeks), will be identified by the investigator. Eligible patients must have no pre-existing heart failure but will be considered at increased risk of developing heart failure due to exposure to potentially cardiotoxic anticancer therapies. Written informed consent will be obtained from all eligible patients prior to enrollment.Patients will receive enalapril at a dose of 5 mg daily for a minimum of three months. The primary objective of this intervention is to evaluate the cardioprotective effects of enalapril in reducing cardiac complications associated with cancer treatment.Following patient identification and obtaining informed consent, treatment allocation will be performed randomly, with patients blinded to their assigned treatment to minimize potential bias in study outcomes. Medication adherence will be carefully assessed throughout the study. Patients with medication adherence below 80% will be withdrawn from the study to maintain the validity and reliability of the final data. Furthermore, adverse events and clinical changes will be regularly monitored throughout the study period.

Category
Prevention

Recruitment centers

1

Recruitment center

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2

Recruitment center

Name of recruitment center
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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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
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Full name of responsible person
Azadeh Moghaddas
Position
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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 2027

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