

Clinical Trial Protocol

Iranian Registry of Clinical Trials

19 Jul 2026

A Phase III, randomized, two-armed, patient-outcome assessor-data analyzer blinded, parallel active controlled non-Inferiority clinical trial study of AryoTrust™ (AryogenTrastuzumab) efficacy and safety in Human Epidermal Growth Factor Receptor 2-Positive breast cancer in comparison to Herceptin® (Genentech/Roche) control.

Protocol summary

Study aim

The aim of this study is to assess non inferiority of AryoTrust (AryoGEN Pharmed) compared to Herceptin (Roche)

Design

This is a Phase III, randomized, two-armed, patient-outcome assessor-data analyzer blinded, parallel active controlled non-Inferiority clinical trial study with a 1:1 allocation

Settings and conduct

This trial will be initiated from July 2016 and 108 patients with breast cancer recruit from the 18 centers. All centers implement same protocol and procedures. Variation of evaluation criteria and schemes will be reduced by investigator meetings, training of personnel in advance of the trial, and by careful monitoring during the trial. After confirmation of the eligibility of the patient and signing the informed consent form, the patients will be allocated to treatment groups according to the trial randomization master sheet (created by CRO Trial). Both products are indistinguishable for patients and health care providers and they will be blind to treatment allocation.

Participants/Inclusion and exclusion criteria

18-70 years old female patients with HER2+ breast cancer, newly diagnosed stage III (locally advanced) or in-operable stage II are candidates for participation.

Intervention groups

This study has two arms with 1:1 allocation. subjects in group I will receive AryoTrust (AryoGen Pharmed) plus Docetaxel every 3 weeks. subjects in group II will receive Herceptin® (Genentech/Roche) plus Docetaxel every 3 weeks. Both groups will receive Doxorubicin + Cyclophosphamid for 4 cycles before randomization.

Main outcome variables

Pathologic Complete Response

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT201606226135N7**

Registration date: **2016-06-25, 1395/04/05**

Registration timing: **prospective**

Last update: **2018-08-16, 1397/05/25**

Update count: **2**

Registration date

2016-06-25, 1395/04/05

Registrant information

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Recruitment status

Recruitment complete

Funding source

All expenses of this study including patients' treatment and medicines, study conduct and performing and research related injuries compensation will be provided

by Aryogen pharmed co.

Expected recruitment start date

2016-07-02, 1395/04/12

Expected recruitment end date

2017-07-03, 1396/04/12

Actual recruitment start date

2016-07-09, 1395/04/19

Actual recruitment end date

2018-06-11, 1397/03/21

Trial completion date

empty

Scientific title

A Phase III, randomized, two-armed, patient-outcome assessor-data analyzer blinded, parallel active controlled non-Inferiority clinical trial study of AryoTrust™ (AryogenTrastuzumab) efficacy and safety in Human Epidermal Growth Factor Receptor 2-Positive breast cancer in comparison to Herceptin® (Genentech/Roche) control.

Public title

Efficacy and safety in AryoTrust™ (Aryogen trastuzumab) vs Herceptin® (Genentech/Roche trastuzumab), a non inferiority trial

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

18-70 years old female patients Patients with newly diagnosed stage III(locally advanced) or in-operable stage II (due to sizes larger than 5 cm or high tumor to breast ratio) tumors are candidates for participation Willing and able to sign an informed consent Pathological diagnosis of adenocarcinoma of the breast ECOG status of 0-1 With any ER/PR status HER2 positive

Exclusion criteria:

Clinical or radiologic evidence of metastatic disease History of any other malignancy including previous breast cancer, second non-breast malignant disease History of previous chemotherapy Left ventricular ejection fraction [LVEF] <55% confirmed by echo cardiogram within 3 months before registration Any prior myocardial infarction, History of documented congestive heart failure (CHF) Any prior history of arrhythmia or cardiac vascular disease requiring medications or clinically significant Current use of medications for treatment of angina pectoris Current uncontrolled hypertension (diastolic > 100 mmHg or systolic > 200 mmHg) A severe conduction abnormality (having pacemaker or diagnosed by the ECG) and any other significant cardiovascular disease Hematologic abnormalities including baseline Absolute NeutrophilCount (ANC) of $\leq 1,500/\mu\text{L}$ or platelet count $\leq 100,000/\mu\text{L}$ Liver dysfunction including : Alanine amino transferase(ALT) and/or aspartate amino transferase (AST) ≥ 3 Upper Limit Normal (ULN), Alkaline phosphatase (ALP) ≥ 3 $\square$ ULN serum, total bilirubin > 1.5 ULN Renal dysfunction, defined as serum creatinin ≥ 2.5 mg/dL Pregnant, lactating women or women of childbearing potential who are not willing to use adequate contraception

Age

From **18 years** old to **70 years** old

Gender

Female

Phase

3

Groups that have been masked

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

Sample size

Target sample size: **108**

Actual sample size reached: **108**

Randomization (investigator's opinion)

Randomized

Randomization description

The randomization is based on blocked randomization. Patient's allocation will be carried on 1:1 allocation ratio by 27 blocks (length of each block is 4). Randomization sequence will be generated using the random generation command in Microsoft Excel (RANDBETWEEN)

Blinding (investigator's opinion)

Triple blinded

Blinding description

Both trastuzumab products are indistinguishable for patients and health care providers. So it will be possible to make patients blind about the treatment group which they have been allocated to. In addition to this, the outcome evaluators and data managers (data analyzer) will not be aware of patients' allocations.

Placebo

Not used

Assignment

Parallel

Other design features**Secondary Ids****1****Registry name**

clinicaltrial.gov

Secondary trial Id

NCT03425656

Registration date

2018-06-02, 1397/03/12

Ethics committees**1****Ethics committee****Name of ethics committee**

Tehran university of medical science, Medical Ethics Committee

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Tehran university of medical science

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1417653761

Approval date

2016-06-22, 1395/04/02

Ethics committee reference number

ir.tums.rec.1395.2730

2**Ethics committee****Name of ethics committee**

Isfahan university of medical science

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Approval date

2016-07-17, 1395/04/27

Ethics committee reference number

IR.MUI.REC.1395.4.041

Health conditions studied**1****Description of health condition studied**

breast cancer patients with HER2-positive

ICD-10 code

C50

ICD-10 code description

Malignant neoplasm of breast

Primary outcomes**1****Description**

pathologic Complete Response (pCR)

Timepoint

following completion of neoadjuvant systemic therapy

Method of measurement

the absence of residual invasive cancer on hematoxylin and eosin evaluation of the complete resected breast specimen and all sampled regional lymph nodes

Secondary outcomes**1****Description**

clinical Complete Response (cCR)

Timepoint

after completion of neoadjuvant systemic therapy

Method of measurement

Disappearance of lesions in imaging. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm

2**Description**

clinical Partial Response (cPR)

Timepoint

after completion of neoadjuvant systemic therapy

Method of measurement

At least a 30% decrease in the sum of diameters of target lesions through imaging

3**Description**

clinically Stable Disease (cSD)

Timepoint

after completion of neoadjuvant systemic therapy

Method of measurement

Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD through imaging

4**Description**

clinical Progressive Disease (cPD)

Timepoint

after completion of neoadjuvant systemic therapy

Method of measurement

at least 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm through imaging

5**Description**

clinical Objective Response(cOR)

Timepoint

after completion of neoadjuvant systemic therapy

Method of measurement

cOR= cCR+ cPR

6**Description**

breast conservation rate

Timepoint

After surgery

Method of measurement

number of mastectomy or Breast conservative surgery

7**Description**

Immunogenicity

Timepoint

Week 10, 13, 19 and 26

Method of measurement

Laboratory results

8

Description

Adverse events

Timepoint

Every cycle

Method of measurement

Laboratory data and patient assessments

Intervention groups

1

Description

Intervention group: All patients are scheduled to receive Doxorubicin + Cyclophosphamide/Docetaxel+AryoTrust regimen as detailed bellow: Doxorubicin + Cyclophosphamide phase: (Cycle length: 14 days.Total cycles: 4) CyclesDoxorubicin, 60 mg/m2 IV + Cyclophosphamide,600 mg/m2 IV. Docetaxel + AryoTrust™ phase: (Cycle length: 21 days.Total cycles: 4 cycles) Docetaxel, 100 mg/m2 IV, AryoTrust™ (Produced by AryoGEN Pharmed) 8 mg/kg IV loading dose (at cycle 1), followed by 6 mg/kg at subsequent cycles

Category

Treatment - Drugs

2

Description

Control Group: All patients are scheduled to receive Doxorubicin + Cyclophosphamide/Docetaxel+Herceptin regimen as detailed bellow: Doxorubicin + Cyclophosphamide phase: (Cycle length: 14 days.Total cycles: 4) CyclesDoxorubicin, 60 mg/m2 IV + Cyclophosphamide,600 mg/m2 IV. Docetaxel + Herceptin phase: (Cycle length: 21 days.Total cycles: 4 cycles) Docetaxel, 100 mg/m2 IV, Herceptin (Produced by Roche) 8 mg/kg IV loading dose (at cycle 1), followed by 6 mg/kg at subsequent cycles

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Khomeini Hospital Complex

Full name of responsible person

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Recruitment center

Name of recruitment center

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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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

Aryogen pharmed Company

Proportion provided by this source

100

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Industry

Person responsible for general inquiries

Contact

Name of organization / entity

Orchid pharmed Company

Full name of responsible person

Somayeh Amini

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)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available