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≤1,500/µL or platelet count ≤ 100,000/µL Liver dysfunction including : Alanine amino transferase(ALT) and/or aspartate amino transferase (AST) ≥3 Upper Limit Normal (ULN), Alkaline phosphatase (ALP) ≥3 □ 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
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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
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Sponsors / Funding sources

1

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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
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

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Latest degree
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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