

Clinical Trial Protocol

Iranian Registry of Clinical Trials

17 Aug 2026

A Randomized parallel group clinical trial to determine the effectiveness, safety and tolerability of Actoverco Filgrastim and Actoverco Pegfilgrastim compared to Neupogen® for prevention of chemotherapy induced neutropenia in the treatment of the breast cancer

Protocol summary

Summary

A major dose-limiting toxicity of chemotherapy is neutropenia and contributes to morbidity associated with cancer. The primary purpose of this study is to establish the effectiveness of a new biosimilar of Filgrastim (Actostim) - as preventive treatment for, Chemotherapy Induced neutropenia compared with the original one (Neupogen) in breast cancer patients. Other purposes of this study are to establish the safety and tolerability of the product. Twenty four hours after chemotherapy, 140 female patients aged 18 to 70 years old who have high risk stage 2 or more of breast cancer and need chemotherapy will randomly be assigned to the study drug. For eligible patients in the first cycle, the injections of Filgrastim will be done by an educated nurse in the center with a single subcutaneous dose (0.5 MIU/kg/day), 24 hours after chemotherapy. Ensuring the patient's ability to perform injections, the labeled drugs will be given to them for the next injections at home, from the second cycle. Results of analyzing will be prepared and presented in form of middle report (upon completion 50% of the sample of the study), and final report (upon completion 100% of the sample of the study).

General information

Acronym

IRCT registration information

IRCT registration number: **IRCT2013042212398N4**
Registration date: **2014-03-17, 1392/12/26**
Registration timing: **registered_while_recruiting**

Last update:

Update count: **0**

Registration date

2014-03-17, 1392/12/26

Registrant information

Name

Farhad Hatami Sadabadi

Name of organization / entity

Actover Pharmaceutical Company

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Recruitment status

Recruitment complete

Funding source

Actover pharmaceutical company

Expected recruitment start date

2014-01-21, 1392/11/01

Expected recruitment end date

2015-07-23, 1394/05/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A Randomized parallel group clinical trial to determine the effectiveness, safety and tolerability of Actoverco Filgrastim and Actoverco Pegfilgrastim compared to Neupogen® for prevention of chemotherapy induced neutropenia in the treatment of the breast cancer

Public title

Determining the effectiveness, safety and tolerability of

Actoverco Filgrastim and Actoverco Pegfilgrastim compared to Neupogen in preventing the chemotherapy induced neutopenia in treatment of the breast cancer

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion Criteria: Female patients aged 18 to 70 years old; Signed informed consent obtained prior to initiation the study; Patients diagnosed having high risk stage 2 or stage 3 and or 4 of breast cancer (by histopathological or cytological diagnosis) and need chemotherapy; A priori has been decided to be treated with G-CSF and subjects eligible for G-CSF therapy according to indications and clinical use in the product monograph; Any acute adverse effects of prior therapy must have resolved to $\leq$ NCI CTCAE (Version 4.0) grade 1 (excluding alopecia) prior to Day 1 of Cycle 1; ECOG Performance Status 0 or 1 as determined on Day 1 of Cycle 1 prior to administration of chemotherapy; Patients must have adequate organ function including the following: a. Adequate bone marrow functions, as determined within 1 day prior to administration of chemotherapy on Day 1 of Cycle 1 and as indicated by: Hb $\geq$ 10 g/dL (transfusion permitted to be included in the trial WBC $\geq$ 3,5 x 10⁹/L, Absolute neutrophil count (ANC) $\geq$ 1.5 x 10⁹/L Platelets $\geq$ 100 x 10⁹/L , b. Adequate renal and hepatic function, as determined within 1 day prior to administration of chemotherapy on Day 1 of Cycle 1 and as indicated by: i. Hepatic: Bilirubin $\leq$ 1.5 x the upper limit of normal (ULN) (unless elevation is known to be due to Gilbert's disease), Subjects must also meet one of the following criteria: ii. a) Alkaline phosphatase within normal reference range and both AST and ALT $>$ 2.5 x ULN; or b) Alkaline phosphatase $<$ 2.5 x ULN and both AST and ALT $<$ 1.5 x ULN; or c) Alkaline phosphatase $<$ 5 x ULN and both AST and ALT within normal reference range; Renal: Serum creatinine $\leq$ 1.5 mg/dL or $\geq$ 90 ml/min GFR; Patients of child-bearing potential must have a negative pregnancy test within 3 days prior to the first dose of chemotherapy (Day 1 of Cycle 1) and use at least one form of contraception as approved by the Investigator for four weeks prior to the study and during the study. For the purposes of this study, child-bearing potential is defined as: "All female patients unless they are post-menopausal for at least one year or are surgically sterile". Acceptable methods of contraception include IUD, oral contraceptive, subdermal implant and double barrier (condom with a contraceptive sponge or contraceptive suppository); Life expectancy more than 3 months; Entering to the study before the second cycle of chemotherapy; Ability to co-operate with the treatment and follow up. Exclusion Criteria: Safety of treatment dependent criteria: Presence of any serious concomitant systemic disorders incompatible with the administration of G-CSF or any systemic disease that can influence the patient's safety (according to doctor's diagnosis); history of hypersensitivity to natural or recombinant G-CSF, or hypersensitivity to human albumin or any other component of the formulation; History of poorly controlled hypertension (BP $>$ 180/110 mmHg) and/or other clinically significant major disease (according to doctor's diagnosis); Serious local infection or active

systemic infection within 10 days prior to enrollment or patients who have taken antibiotics within the previous 10 days; Pregnant or breast-feeding patients; Cardiac insufficiency, cardiomyopathy, significant cardiac dysrhythmia, unstable or advanced ischemic heart disease (NYHA III or IV; Known bleeding disorder Criteria dependent on compliance with study procedures, or the evaluation of the response: Unwilling to use a reliable and acceptable contraceptive method throughout the study period (fertile patients only); Treatment with certain other agents to treat the malignant disease; Patients requiring autologous or allogeneic stem cell transplantation; Patients receiving simultaneous radiotherapy; Patients who have taken colony stimulation factor within the previous 10 days; Treatment with any investigational product within 30 days prior to study drug administration; Previous participation in this study; Having chemotherapy for any reason in the last 5 years and or receiving $>$ 240 mg/m² doxorubicin or $>$ 600 mg/m² Epirubicin at the life time; Already involved in this research project.

Age

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

Gender

Female

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **156**

Randomization (investigator's opinion)

Randomized

Randomization description

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Iran University of Medical Sciences

Street address

Next to Milad Hospital, between the intersection of Sheykh Fazl Allah Nuri and Chamran, Hemmat Highway.

City

Tehran

Postal code

1449614535

Approval date

2014-12-02, 1393/09/11

Ethics committee reference number

93-d-105-4251

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

breast cancer

ICD-10 code

C50

ICD-10 code description

breast cancer

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

Duration of Severe Neutropenia

Timepoint

The number of days that patients have severe neutropenia (defined as above)

Method of measurement

Daily Hematology During severe neutropenia

2**Description**

Severe Neutropenia

Timepoint

before intervention, from day 6 to 14 after chemotherapy in first cycle

Method of measurement

Hematology

3**Description**

Drug intolerance

Timepoint

14 and 21 days after intervention in each cycle

Method of measurement

Doctor`s diagnosis

4**Description**

Febrile neutropenia

Timepoint

before intervention, day 7 and 14 after chemotherapy in each cycle and 30 days after the last dose of chemotherapy.

Method of measurement

Physical exam and Para clinic

5**Description**

Serious adverse events

Timepoint

Whenever it happens

Method of measurement

Doctor`s observation and report

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

Fever

Timepoint

before intervention, from day 6 to 14 after chemotherapy in first cycle, day 14 after chemotherapy in second till forth cycle and 30 days after the last dose of chemotherapy.

Method of measurement

Thermometer

2**Description**

Fever duration

Timepoint

Whenever a patient has fever

Method of measurement

Physical exam

3**Description**

Height

Timepoint

before intervention

Method of measurement

Meter

4**Description**

ANC

Timepoint

before intervention, from day 6 to 14 after chemotherapy in first cycle, day 7 and 14 after chemotherapy in second till forth cycle and 30 days after the last dose of chemotherapy.

Method of measurement

multiplied the percentage of neutrophils in the WBC count

5**Description**

Ability to continue chemotherapy

Timepoint

14 days after chemotherapy in each cycle

Method of measurement

Doctor`s Report

6**Description**

Weight

Timepoint

before intervention, 14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy.

Method of measurement

Carriage scales

7**Description**

Bone pain

Timepoint

before intervention, 14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy

Method of measurement

According to patient's Statement

8**Description**

Non-life-threatening side effects

Timepoint

14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy

Method of measurement

Doctor's observation and report

9**Description**

Severity of bone pain

Timepoint

14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy

Method of measurement

according to VAS criteria

10**Description**

Age

Timepoint

before intervention

Method of measurement

According to birthday

11**Description**

race

Timepoint

before intervention

Method of measurement

According to patient's Statement

12**Description**

Laboratory abnormalities

Timepoint

Before intervention, from day 6 to 14 after chemotherapy in first cycle, day 7 and 14 after chemotherapy in second till forth cycle and 30 days after the last dose of chemotherapy.

Method of measurement

Hematology

13**Description**

Hospitalization

Timepoint

Whenever needed during the study

Method of measurement

Doctor's diagnosis

14**Description**

Duration of Hospitalization

Timepoint

Duration of Hospitalization at any time patient hospitalized

Method of measurement

Review of patient records

15**Description**

Infection

Timepoint

14 days after intervention in each cycle

Method of measurement

Physical exam and Paraclinic

16**Description**

need for intravenous antibiotics

Timepoint

14 days after chemotherapy in each cycle

Method of measurement

Doctor's prescription

17**Description**

the injection site Pain

Timepoint

14 and 21 days after intervention in each cycle and 28 days after the end of the study

Method of measurement

According to patient's Statement

18**Description**

Severity of the injection site pain

Timepoint

14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy.

Method of measurement

according to VAS criteria

19**Description**

Functional status

Timepoint

before intervention, 14 days after chemotherapy in each cycle and 30 days after the last dose of chemotherapy.

Method of measurement

ECOG criteria

20**Description**

Exit the study for any reason

Timepoint

Whenever it happens

Method of measurement

Doctor or patient's Statement

21**Description**

Excluded reason

Timepoint

Whenever it happens

Method of measurement

Doctor or patient's Statement

22**Description**

Dosage of chemotherapy

Timepoint

14 days after intervention in each cycle.

Method of measurement

Doctor's prescription

23**Description**

Stage of breast cancer

Timepoint

before intervention

Method of measurement

TNM criteria

24**Description**

Drug

Timepoint

before intervention

Method of measurement

BBR Table

Intervention groups**1****Description**

Intervention group: Twenty four hours after each cycle of chemotherapy, injections of filgrastim (0.5 mIU/kg/day until post nadir ANC recovery) or Pegfilgrastim (6 mg, single dose) will be done. Protocol of chemotherapy drugs On the first day of each cycle: On the first day of each cycle associated to AC regimen, patients receive an IV bolus of Doxorubicin (60 mg/m² IV) in 20 min and then

Cyclophosphamide (600mg/m²) in 30 minutes. AC regimen is repeated every 14 days for 4 cycles and then followed by Paclitaxel regimen. Patients receive a three-hour Paclitaxel (175 mg/m² IV) every 14 days for 4 cycles. There is no indication for G-CSF support in cycles 5 to 8 due to lower toxicity of Paclitaxel.

Category

Treatment - Drugs

2**Description**

Control group: Twenty four hours after each cycle of chemotherapy, injections of Neopogen (0.5 mIU/kg/day until post nadir ANC recovery) will be done. Protocol of chemotherapy drugs On the first day of each cycle: On the first day of each cycle associated to AC regimen, patients receive an IV bolus of Doxorubicin (60 mg/m² IV) in 20 min and then Cyclophosphamide (600mg/m²) in 30 minutes. AC regimen is repeated every 14 days for 4 cycles and then followed by Paclitaxel regimen. Patients receive a three-hour Paclitaxel (175 mg/m² IV) every 14 days for 4 cycles. There is no indication for G-CSF support in cycles 5 to 8 due to lower toxicity of Paclitaxel.

Category

Treatment - Drugs

Recruitment centers**1****Recruitment center****Name of recruitment center**

FIROUZGAR Hospital

Full name of responsible person

Dr Asiyeh Ghorbani

Street address

Hematology Oncology department of FIROUZGAR hospital, before VALI-ASR Sq.

City

Tehran

Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Actoverco Pharmaceutic Company

Full name of responsible person

Dr Farhad Hatami Sadabadi

Street address

No. 17, 20 metri dasht behesht st., SA-ADAT ABAD

City

Tehran

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

Yes

Title of funding source

Actoverco Pharmaceutic Company
Proportion provided by this source
100
Public or private sector
empty
Domestic or foreign origin
empty
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
empty

Person responsible for general inquiries

Contact

Name of organization / entity
ACTOVERCO Pharmaceutical Company
Full name of responsible person
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
empty
Study Protocol
empty
Statistical Analysis Plan
empty
Informed Consent Form
empty
Clinical Study Report
empty
Analytic Code
empty
Data Dictionary
empty