Clinical Trial Protocol
Iranian Registry of Clinical Trials

18 Sep 2026

A Phase III, randomized, two-armed, double-blind (patient and assessor blinded), parallel active controlled non-Inferiority clinical trial to evaluate the efficacy and safety of bevacizumab(AryoGen®) plus FOLFIRI-3 in comparison with bevacizumab (Avastin®) plus FOLFIRI-3 as a first line therapy in patients with metastatic colorectal cancer (mCRC)

Protocol summary

Study aim

The purpose of this study was to compare the efficacy and safety of the proposed bevacizumab biosimilar to the reference product in patients with metastatic colorectal cancer mCRC

Design

This phase III, randomized, two-armed, parallel, double-blinded (patient- and assessor-blinded), active-controlled, multicenter, noninferiority study was conducted in 22 centers across nine cities of Iran. The randomization plan of the 126 patients will be carried out using an on-line system (http://www.randomization.com).

Settings and conduct

This phase III, randomized, two-armed, parallel, double-blinded (patient- and assessor-blinded), active-controlled, multicenter, noninferiority study was conducted in 22 centers across nine cities of Iran

Participants/Inclusion and exclusion criteria

According to criteria

Intervention groups

Study Drug(Arm A): FOLFIRI3 , Bevacizumab (AryoGen Pharmed) Control (Arm B): FOLFIRI3 , Bevacizumab (Avastin)

Main outcome variables

The primary endpoint was progression-free survival (PFS), which was defined as the time from the date of randomization to the first date of documented progression or death as a result of any cause.1 year after randomization

General information

Reason for update

Updating the inclusion and exclusion data, updating of centers, editing of primary and secondary outcome

Acronym

IRCT registration information

IRCT registration number: **IRCT2015072517994N2**
Registration date: **2016-07-28, 1395/05/07**
Registration timing: **prospective**

Last update: **2020-11-19, 1399/08/29**
Update count: **1**

Registration date

2016-07-28, 1395/05/07

Registrant information

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Recruitment status

Recruitment complete

Funding source

AryoGen Pharmed Company

Expected recruitment start date

2016-08-22, 1395/06/01

Expected recruitment end date

2016-08-22, 1395/06/01

Actual recruitment start date

2016-10-04, 1395/07/13

Actual recruitment end date
2017-07-30, 1396/05/08
Trial completion date
2018-07-30, 1397/05/08

Scientific title
A Phase III, randomized, two-armed, double-blind (patient and assessor blinded), parallel active controlled non-Inferiority clinical trial to evaluate the efficacy and safety of bevacizumab(AryoGen®) plus FOLFIRI-3 in comparison with bevacizumab (Avastin®) plus FOLFIRI-3 as a first line therapy in patients with metastatic colorectal cancer (mCRC)

Public title
Evaluation the efficacy and safety of bevacizumab in comparison with bevacizumab (Avastin®) as a first line therapy in patients with metastatic colorectal cancer (mCRC)
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Inclusion criteria: Male or female aged 18-75 years at the time of signing the informed consent form, have been diagnosed as mCRC verified histologically, having one or more bi-dimensionally measurable lesions as defined by Response Evaluation Criteria In Solid Tumors (RECIST) criteria, was not felt to be amenable to curative resection, with an Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 1, life expectancy of longer than 3 months (clinical assessment), adequate organ and marrow function as defined below: Absolute neutrophil count (ANC) greater than/equal to 1,500/mm3; o Platelets greater than/equal to 100,000/ mm3; o Hemoglobin greater than/equal to 9 gm/dl (may be transfused to maintain or exceed this level); o Total bilirubin less than/equal to 1.5 within institutional upper limit of normal (IULN); Aspartate aminotransferase (AST or SGOT)/alanine aminotransferase (ALT or SGPT) less than/equal to 2.5 times IULN, or less than/equal to 5 times IULN if known liver metastases, may have received adjuvant therapy for primary colorectal cancer provided that at least 6 months have elapsed from the time the adjuvant therapy was concluded and recurrent disease was documented, Patients with history of hypertension must be well-controlled (blood pressure less than/equal to 150/100mmHg), on a stable regimen of anti-hypertensive therapy.
Exclusion criteria:
Exclusion criteria, Radiotherapy or surgery for mCRC less than 4 weeks before random assignment, Undergone major surgical procedures or open biopsy within 28 days before the initiation of study treatment, experienced a significant traumatic injury, within 28 days before study entry, currently using or had recently used therapeutic anticoagulants, thrombolytic therapy, chronic, daily treatment with aspirin(higher than 325 mg/daily). (Patients may have prophylactic use of low molecular weight heparin, however therapeutic use of heparin or low molecular weight heparin is not acceptable) - Proteinuria exceeding 500mg/24h - History or presence of central nervous system metastases - Female patients who are pregnant or lactating - Patients with a history of allergic reactions attributed to compounds of similar chemical or biologic composition to bevacizumab, irinotecan, 5-FU, or leucovorin - Serious non-healing wound, ulcer, or an active bone fracture - Patients with any history of another primary malignancy less than/equal to 5 years, with the exception of non-melanoma skin cancer, and carcinoma in situ of the uterine cervix. - Myocardial infarction within 6 months before of study enrollment; - History of stroke within 6 months before of study enrollment; - Unstable symptomatic arrhythmia requiring medication; - Clinically significant peripheral vascular disease; - Uncontrolled diabetes; Serious active or uncontrolled infection - Inability to comply with study and/or follow-up procedures
Age
From **18 years** old to **75 years** old
Gender
Both

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **126**
Actual sample size reached: **126**
Randomization (investigator's opinion)
Randomized
Randomization description
The randomization plan of the patients will be carried out using an on-line system (http://www.randomization.com). Using permuted block randomization (length of each block is 6) will be made, for a total of 126 patients (with 2:1 allocation ratio). Once the randomization has been made, each patient is given a code with which he will be identified throughout the study. The assigned code will be denoted by 4 initials (corresponding to the 2 first letter of the first name, the 2 first letter of the first surname), and 3 numbers (center code). Moreover, the code described is followed by study unique identification consisting of the first two letters of the generic name and study phase, respectively (which is BE3-) and 4 numbers (corresponding to the randomization number), e.g. ABCD001BE3-0001. The randomization number will be assigned in a consecutive way.
Blinding (investigator's opinion)
Double blinded
Blinding description
Each study's drug package for the course of a patient's treatment had a 3-digit number similar to the randomization code, so as long as the random code was unique, each patient had a unique drug package that will be completely identified with the randomized process.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

1

Registry name
ClinicalTrials.gov
Secondary trial Id
NCT03288987
Registration date
2018-07-30, 1397/05/08

Ethics committees

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Ethics committee
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2016-06-21, 1395/04/01
Ethics committee reference number
IR.SBMU.REC.1395.4

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Approval date
2016-08-24, 1395/06/03
Ethics committee reference number
IR.AJUMS.REC.1395.351

Health conditions studied

1

Description of health condition studied
Metastatic colorectal cancer
ICD-10 code
C18-9
ICD-10 code description
Malignant neoplasm of colon

Primary outcomes

1

Description
progression-free survival
Timepoint
1 year after randomization
Method of measurement
Method of measurement: the time from the date of randomization to the first date of documentation progression (per investigator assessment) or death as a result of any cause.

Secondary outcomes

1

Description
Overall survival: the time from date of randomization to date of death due to any cause.Overall response rate: partial and complete responses, according to the RECIST criteria.Time to treatment failure: as the time from the date of randomization to the date of each of the following: The treatment modalities did not destroy or modify the cancer cell, the tumor either became larger (disease progression) or stayed the same size after treatment, Death from any cause, Discontinuation of treatment.Safety: Safety will be assessed based on adverse events reports, the results of laboratory tests, vital signs and immunogenicity. All adverse events are categorized by CTCAE (v. 5.0) guideline of the American National Cancer Institute.
Timepoint
During one year after randomization
Method of measurement
time based on month, RESICT guidline

Intervention groups

1

Description
Intervention (Arm A): FOLFIRI - 3+bevacizumab(AryoGen®) FOLFIRI - 3: In this group FOLFIRI-3 regimen consists of irinotecan 100 mg/m2 over 1 hour at day 1, leucovorin 400 mg/m2 at day 1 followed by a 46 hour 5-FU continuous infusion (2400 mg/m2), and irinotecan 100 mg/m2 over 1 hour at day 3 will administer. Drug: Bevacizumab (AryoGen ®) 5 mg/kg will administer every 2 weeks. Initially, it will administer as a 90 min infusion. If the first infusion is well-tolerated, the second will deliver as a 60 min infusion; if the 60-min infusion is well tolerated; all subsequent infusions will deliver over 30 min
Category
Treatment - Drugs

2

Description
Active Comparator(Arm B) FOLFIRI - 3 + Bevacizumab

(Avastin) FOLFIRI-3: In this group FOLFIRI-3 regimen consist of irinotecan 100 mg/m2 over 1 hour at day 1, leucovorin 400 mg/m2 at day 1 followed by a 46 hour 5-FU continuous infusion (2400 mg/m2), and irinotecan 100 mg/m2 over 1 hour at day 3 will administer. Drug: Bevacizumab (Avastin) 5 mg/kg will administer every 2 weeks. Initially it will administer as a 90 min infusion. If the first infusion is well tolerated, the second will deliver as a 60 min infusion; if the 60-min infusion is well tolerated; all subsequent infusions will deliver over 30 min

Category

Treatment - Drugs

Recruitment centers

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Sponsors / Funding sources

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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
Aryogene 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

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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