Clinical Trial Protocol
Iranian Registry of Clinical Trials

13 Jun 2026

A Phase III, randomized, two armed, parallel, double blind, active controlled, equivalency clinical trial to determine the therapeutic efficacy and safety between Cetuximab (produced by CinnaGen) and FOLFIRI compared with Erbitux® (Cetuximab, the reference drug, produced by Merck Company) and FOLFIRI as first-line treatment for RAS wild-type Metastatic Colorectal Cancer

Protocol summary

Study aim

The aim of this study is to determine the equivalency of efficacy and safety of cetuximab (CinnaGen) versus Erbitux® (Merck) in progression free survival (PFS) when added to FOLFIRI (irinotecan plus leucovorin/ 5-fluorouracil continuous infusion) in patients with metastatic colorectal cancer (mCRC) without mutations in RAS genes

Design

A phase III, Active-controlled, Parallel, double-blind, randomized clinical trial

Settings and conduct

This is a multicenter, double-blinded study.

Participants/Inclusion and exclusion criteria

Inclusion: • Age of 18 years or older • Histologically confirmed adenocarcinoma of the colon or rectum • Having one or more bi-dimensionally measurable lesions as defined by RECIST Criteria • Adequate organ and marrow function Exclusion: • Previous exposure to an anti-EGFR therapy or irinotecan-based chemotherapy • Adjuvant treatment that was terminated 6 months or less before the start of treatment in our trial • The use of radiotherapy, surgery (excluding previous diagnostic biopsy), or any investigational drug in the 30-day period before the start of treatment in our trial • Female patients who are pregnant or lactating chemically or biologically similar to Cetuximab, irinotecan, 5-FU or leucovorin. • Patients with a history of another primary malignancy in less than 5 years, • Inability to comply with study and/or follow-up procedures

Intervention groups

Cetuximab 400 mg/m2 for the first and 250 mg/m2 for subsequent doses

Main outcome variables

Primary Endpoint: Progression Free Survival Secondary Endpoints: Overall Survival, Time to Treatment Failure, Objective Response Rate, Safety, and Immunogenicity.

General information

Reason for update

updating and changing of the Colorectal metastatic cancer treatment guideline

Acronym

IRCT registration information

IRCT registration number: **IRCT2017110821315N10**
Registration date: **2017-11-15, 1396/08/24**
Registration timing: **prospective**

Last update: **2024-02-20, 1402/12/01**
Update count: **3**

Registration date

2017-11-15, 1396/08/24

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Recruitment status

Recruitment complete

Funding source
CinnaGen Company

Expected recruitment start date
2017-11-30, 1396/09/09
Expected recruitment end date
2025-03-19, 1403/12/29
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A Phase III, randomized, two armed, parallel, double blind, active controlled, equivalency clinical trial to determine the therapeutic efficacy and safety between Cetuximab (produced by CinnaGen) and FOLFIRI compared with Erbitux® (Cetuximab, the reference drug, produced by Merck Company) and FOLFIRI as first-line treatment for RAS wild-type Metastatic Colorectal Cancer

Public title
An equivalency clinical trial to determine the efficacy and safety between Cetuximab (produced by CinnaGen) compared with Erbitux® in RAS wild-type Metastatic Colorectal Cancer
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
male or female Age of 18 till 75 histologically confirmed adenocarcinoma of the colon or rectum having one or more bi-dimensionally measurable lesions as defined by Response Evaluation Criteria in Solid Tumors (RECIST) Criteria metastatic disease that could not be resected for curative purposes immunohistochemical evidence of tumor EGFR expression (expanded wild-type RAS) Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or less life expectancy of longer than 3 months (by clinical assessment) adequate organ and marrow function.
Exclusion criteria:
Previous exposure to an anti-EGFR therapy or irinotecan-based chemotherapy the use of radiotherapy, surgery (excluding previous diagnostic biopsy), or any investigational drug in the 30-day period before the start of treatment in our trial female patients who are pregnant or lactating patients with a history of another primary malignancy in less than 5 years, with the exception of non-melanoma skin cancer and carcinoma in-situ of uterine cervix patients with history of allergic reactions attributed to compounds chemically or biologically similar to Cetuximab, irinotecan, 5-FU or leucovorin adjuvant treatment that was terminated 6 months or less before the start of treatment in our trial inability to comply with study and/or follow-up procedures Subjects with known infection with HIV, HBV, HCV first line treatment in patient with right sided primary tumor
Age
From **18 years** old to **75 years** old

Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator

Sample size
Target sample size: **234**
Randomization (investigator's opinion)
Randomized
Randomization description
Eligible patients will be assigned to treatment with the use of a dynamic randomization algorithm that will be designed to achieve overall balance between groups; randomization will be stratified according to site of primary tumor and number of metastasis (1 or more than 1) with 1:2 allocation ratio. After randomization procedure, a code will be allocated to each patient that will be used as patient identifier 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 first three letters of the generic name (which is CET-) and 3 numbers (corresponding to the randomization number), e.g. ABCD001CET-001. The randomization number will be assigned in a consecutive way. concealment process: Randomization will not be exposed to those conducting the study and will be provided in sealed opaque envelopes with successive numbers. The original paper of randomized remains in the CRO Trial and after checking eligibility criteria, the randomization code is given to the prescriber by telephone. Randomization will not be exposed to the trial executers and will be provided to the researcher of each center in non-transparent sealed envelopes.
Blinding (investigator's opinion)
Double blinded
Blinding description
Both cetuximab products are indistinguishable for patients and health care providers. Since the route of administration is infusion, and the size and shape of the vial, cap, seal, aluminum and the color are quite similar, it is not possible to distinguish the type of brand from the appearance of vials and it will be possible to make patients blind about the treatment group which they have been allocated to
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

1

Registry name
ClinicalTrial.gov
Secondary trial Id
NCT03391934
Registration date
2017-12-31, 1396/10/10

Ethics committees

1

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Ethics committee reference number
IR.SBMU.REC.1396.228

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Ethics committee reference number
IR.TABRIZ.REC.1396.603

Health conditions studied

1

Description of health condition studied
RAS wild-type Metastatic Colorectal Cancer
ICD-10 code
C18.9, C20
ICD-10 code description
Malignant neoplasm of colon, Malignant neoplasm of rectum

Primary outcomes

1

Description
Assessment of Progression-Free Survival (PFS) time of Cetuximab and Erbitux®
Timepoint
a 12-month period
Method of measurement
PFS is defined as 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
Timepoint
a 12-month period
Method of measurement
the time from date of randomization to date of death due to any cause

2

Description
Objective response rate
Timepoint
a 12-month period
Method of measurement
RECIST criteria (Response Evaluation Criteria in Solid Tumors)

3

Description
Time to treatment failure
Timepoint
a 12-month period
Method of measurement
- Time of treatment failures define 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

4

Description
Safety and frequency of AEs
Timepoint
a 12-month period
Method of measurement
Safety wills assess on the basis of reports of adverse events, laboratory-test results, and vital sign measurements

5

Description
Immunogenicity
Timepoint
Weeks 1, 2, 4, 10, 16, 22, 28, 34, 40 and 46
Method of measurement
assessment (antidrug antibody [ADA] and neutralizing antibody [nAb])

Intervention groups

1

Description
CinnaGen Cetuximab (produced by CinnaGen) 400 mg/m2 for the first infusion, then weekly intravenous infusions of 250 mg/m2, every week for 6 months
Category
Treatment - Drugs

2

Description
Erbitux® 400 mg/m2 for the first infusion, then weekly intravenous infusions of 250 mg/m2, every week for 6 months
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
CinnaGen 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

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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