Clinical Trial Protocol
Iranian Registry of Clinical Trials

08 Oct 2026

Comparison of pathological response rates in long-term chemoradiotherapy versus short-term radiotherapy in the total neoadjuvant treatment of patients with locally advanced rectal cancer in the context of a randomized clinical trial

Protocol summary

Study aim

Evaluation of pathologic response following long-course chemoradiotherapy versus short-course radiotherapy in total neoadjuvant treatment of patients with locally advanced rectal cance

Design

Randomized clinical trial, parallel-group, phase 2. In this study, patients are allocated to two treatment groups (Group A: long-course chemoradiation, Group B: short-course radiotherapy). Randomization is performed using the RAND function in Microsoft Excel. The total sample size is 60 patients (30 patients per group).

Settings and conduct

This study is a phase 2 randomized clinical trial conducted at Shahid Rajaei Hospital, Babolsar, Iran. Eligible patients with locally advanced rectal adenocarcinoma are recruited from the hospital's oncology and colorectal surgery clinics.

Participants/Inclusion and exclusion criteria

Patients aged over 18 years with locally advanced rectal adenocarcinoma located within 16 cm from the anal verge, who are clinically eligible for surgery following neoadjuvant treatment, and who do not meet any of the exclusion criteria—including histology other than adenocarcinoma, synchronous adenocarcinoma elsewhere in the colon, history of prior malignancy (except basal cell carcinoma of the skin), prior chemotherapy, prior pelvic radiotherapy, inflammatory bowel disease, or bilateral hip prostheses—will be eligible for inclusion in the study.

Intervention groups

patients aged ≥18 years with biopsy-confirmed rectal adenocarcinoma located ≤16 cm from the anal verge, clinical stage cT3–T4 or regional lymph node-positive, ECOG 0–2, without distant metastasis, and meeting standard laboratory criteria. Patients with synchronous colorectal cancer, prior malignancy (except BCC), prior chemotherapy or pelvic radiotherapy, inflammatory bowel disease, or bilateral hip prostheses will be excluded.

Main outcome variables

Pathologic complete response, pCR

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20251017067655N1**
Registration date: **2025-12-28, 1404/10/07**
Registration timing: **registered_while_recruiting**

Last update: **2025-12-28, 1404/10/07**
Update count: **0**

Registration date

2025-12-28, 1404/10/07

Registrant information

Name
Shabnam AshofteBargi
Name of organization / entity
Country
Iran (Islamic Republic of)
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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-10-16, 1404/07/24

Expected recruitment end date

2026-01-20, 1404/10/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of pathological response rates in long-term chemoradiotherapy versus short-term radiotherapy in the total neoadjuvant treatment of patients with locally advanced rectal cancer in the context of a randomized clinical trial

Public title

Evaluation of the effect of total neoadjuvant therapy in rectal cancer

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Histopathologic confirmation of rectal adenocarcinoma Clinical stage cT3–T4 and/or presence of MRI-defined positive lymph nodes ECOG performance status of 0–2 Adequate bone marrow function (hemoglobin > 10 g/dL; white blood cell count > 3 × 10^9/L; absolute neutrophil count > 1.5 × 10^9/L; platelet count > 100 × 10^9/L Adequate hepatic function (SGOT and/or SGPT ≤ 3 × the upper limit of normal) Adequate renal function (serum creatinine < 1.6 mg/dL)

Exclusion criteria:

Refusal to provide informed consent for study participation Synchronous adenocarcinoma in other segments of the colon Presence of distant metastasis at initial diagnosis History of prior malignancy, except for basal cell carcinoma (BCC) of the skin History of prior chemotherapy History of prior pelvic radiotherapy Inflammatory bowel disease Bilateral hip prostheses

Age

From **18 years** old

Gender

Both

Phase

1-2

Groups that have been masked

No information

Sample size

Target sample size: **60**

Randomization (investigator's opinion)

Randomized

Randomization description

In this study, a blocked randomization method with double and quadruple permutations will be used to allocate patients to the two groups. In this method, two- and four-patient blocks, each comprising combinations of the two treatment arms, are created. To prevent predictability of future treatment assignments, the order of the blocks is determined using a random number table. Accordingly, for a sample size of 60 patients, ten four-patient blocks will be selected from the combinations AABB, ABAB, ABBA, BABA, BBAA, and BAAB, and ten two-patient blocks will be selected from the combinations AB and BA, using a random number table.

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

Ethics committee of babol University of Medical Sciences

Street address

ganj afruz Ave, babol university of medical science

City

babo

Province

Mazandaran

Postal code

4717647745

Approval date

2025-10-15, 1404/07/23

Ethics committee reference number

IR.MUBABOL.REC.1404.136

Health conditions studied

1

Description of health condition studied

Rectal Cancer

ICD-10 code

C20

ICD-10 code description

Malignant neoplasm of rectum

Primary outcomes

1

Description

Pathologic complete response (pCR): The proportion of patients with no viable tumor cells in the resected rectum and regional lymph nodes following total neoadjuvant therapy and surgery.

Timepoint

end of treatment at the time of surgery

Method of measurement

Histopathological evaluation of surgical specimens (TME: APR or LAR) by an experienced pathologist.

Secondary outcomes

1

Description

Acute treatment-related toxicities: Including anemia, neutropenia, thrombocytopenia, diarrhea, nausea/vomiting, anorexia, dysuria, and other adverse events graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Timepoint

Weekly clinical and laboratory evaluation during radiotherapy and every 2–3 weeks during chemotherapy.

Method of measurement

CBC, medical history and physical exam

Intervention groups

1

Description

Intervention group: patients initially receive neoadjuvant induction chemotherapy consisting of one of the following regimens—FOLFOX-4, mFOLFOX-6, or CapOx—for 3 to 4 cycles, according to the treating physician’s discretion.In Group A, 11–18 days after completion of induction chemotherapy, patients undergo long-course chemoradiotherapy, consisting of radiotherapy to a total dose of 50–50.4 Gy delivered in 25–28 daily fractions, with concurrent oral capecitabine at a dose of 825 mg/m² on radiotherapy days. Subsequently, after an interval of 11–18 days, patients receive consolidation chemotherapy using the same regimens.After completion of total neoadjuvant therapy, patients undergo total mesorectal excision (TME) 2–4 weeks after the final cycle of chemotherapy. Abdominoperineal resection (APR) is performed for low rectal tumors, and low anterior resection (LAR) for mid and upper rectal tumors.The clinical target volume (CTV) for radiotherapy includes the primary tumor, the entire mesorectum, and regional lymph nodes in accordance with RTOG guidelines. Radiotherapy boost to the primary tumor with a 1-cm margin may be delivered at the treating physician’s discretion.

Category

Treatment - Other

2

Description

Intervention group: patients initially receive neoadjuvant induction chemotherapy consisting of one of the following regimens—FOLFOX-4, mFOLFOX-6, or CapOx—for 3 to 4 cycles, according to the treating physician’s discretion.In Group B, following induction chemotherapy, patients receive short-course radiotherapy consisting of 5 Gy per fraction for 5 fractions over 5 days (maximum 8 days). After an interval of 11–18 days, consolidation chemotherapy with either a FOLFOX-based regimen or CapOx is administered.After completion of total neoadjuvant therapy, patients undergo total mesorectal excision (TME) 2–4 weeks after the final cycle of chemotherapy. Abdominoperineal resection (APR) is performed for low rectal tumors, and low anterior resection (LAR) for mid and upper rectal tumors.The clinical target volume (CTV) for radiotherapy includes the primary tumor, the entire mesorectum, and regional lymph nodes in accordance with RTOG guidelines. Radiotherapy boost to the primary tumor with a 1-cm margin may be delivered at the treating physician’s discretion.

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

Rajaee hospital

Full name of responsible person

Shabnam Ashoftebargi

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Shariati Street, Shilat Square, Rajaee hospital

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Babol University of Medical Sciences

Full name of responsible person

reza ghadimi

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ghanj afruz Ave, babol university of medical science

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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

Babol University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Babol University of Medical Sciences

Full name of responsible person

Shabnam AshofteBargi

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Radiotherapy

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Person responsible for scientific inquiries

Contact

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Full name of responsible person

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Position

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

In this study, anonymized raw and processed data will be collected, including patient demographic characteristics, tumor features, details of neoadjuvant treatment (chemotherapy and radiotherapy), surgical findings, pathological outcomes (including pathological complete response), and treatment-related outcomes and toxicities. In addition, the study protocol, data collection forms, and final statistical analysis reports will be available for sharing. After completion of the study and publication of the results, de-identified data will be

shared exclusively for research purposes upon formal request and approval by the principal investigator. Data sharing will be conducted in compliance with ethical standards, patient confidentiality, and non-commercial use policies.

When the data will become available and for how long

Start of access period: 6 months after publication of the results

To whom data/document is available

Researchers affiliated with academic and scientific institutions

Under which criteria data/document could be used

The data and documents generated in this study will be available solely for scientific research purposes, including secondary analyses, systematic reviews, and meta-analyses, with the aim of advancing scientific knowledge in the field of rectal cancer treatment. Access to the data will be granted upon formal request and approval by the principal investigator, subject to compliance with research ethics principles, protection of patient confidentiality, and complete anonymization of participant information. The data may be used exclusively for non-commercial and academic research purposes.

From where data/document is obtainable

shabnam Ashofte 09353413556

What processes are involved for a request to access data/document

All requests for access to the study data or documents must be submitted in writing to the principal investigator. Upon receipt, the principal investigator will review and evaluate the request, and if approved, access to the data will be provided in anonymized files, in compliance with confidentiality and research ethics principles. All use of the data is strictly limited to research and non-commercial purposes, and recipients are required to adhere to the terms of use and not disclose any identifiable patient information.”

Comments