N1048

A Phase II/III Trial of Neoadjuvant FOLFOX With Selective Use of Combined Modality Chemoradiation Versus Preoperative Combined Modality Chemoradiation for Locally Advanced Rectal Cancer Patients Undergoing Low Anterior Resection With Total Mesorectal Excision (PROSPECT)

ClinicalTrials.gov Identifier: NCT01515787

Study Background

Trial Description

The standard treatment for locally advanced rectal cancer involves chemotherapy and radiation, known as 5FUCMT, (the chemotherapy drugs 5-fluorouracil/capecitabine and radiation therapy) prior to surgery. Although radiation therapy to the pelvis has been a standard and important part of treatment for rectal cancer and has been shown to decrease the risk of the cancer coming back in the same area in the pelvis, some patients experience undesirable side effects from the radiation and there have been important advances in chemotherapy, surgery, and radiation which may be of benefit. The purpose of this study is to compare the effects, both good and bad, of the standard treatment of chemotherapy and radiation to chemotherapy using a combination regimen known as FOLFOX, (the drugs 5-fluorouracil (5-FU), oxaliplatin and leucovorin) and selective use of the standard treatment, depending on response to the FOLFOX. The drugs in the FOLFOX regimen are all FDA (Food and Drug Administration) approved and have been used routinely to treat patients with advanced colorectal cancer.

Arms:

Group 1: (Experimental): Patients will receive FOLFOX chemotherapy once every two weeks for 6 cycles total over a period of 12 weeks. After completing FOLFOX chemotherapy, the patient will have an MRI scan or endorectal ultrasound (ERUS) to examine the tumor. If the tumor has not decreased in size by at least 20%, the patient will receive 5FUCMT (radiation with chemotherapy). If the tumor has decreased in size by 20%, then the patient will proceed directly to surgery. If all borders of the tumor are normal post surgery, then the patient receives six additional cycles of FOLFOX chemotherapy. If all borders of the tumor are not normal then the patient receives chemoradiation therapy for 5.5 weeks after surgery. After chemoradiation, additional cycles of FOLFOX or similar chemotherapy

will be recommended for 4 cycles or 8 weeks. Patient observation with follow up evaluations and event monitoring will occur up to 8 years post randomization.

Group 2: (Active Comparator): Patients receive 5FUCMT including chemotherapy and radiation therapy for 5.5 weeks. Patients will be given either 5-fluorouracil or capecitabine and radiation therapy. After the chemoradiation therapy is completed, patients will proceed directly to surgery. Post-surgery, patients will receive FOLFOX chemotherapy once every two weeks for 8 cycles total over a period of 16 weeks. Patient observation with follow up evaluations and event monitoring will occur up to 8 years post randomization.

Objectives:

- OUTLINE:
  This is a multicenter, phase II/III study. Patients are stratified according to ECOG performance status (0 or 1 vs 2) and randomized to 1 of 2 treatment regimens. Patients will receive full supportive care while on this study.
  OBJECTIVES:
  Primary
  1. Phase II component: To assure that neoadjuvant FOLFOX followed by selective use of 5FUCMT group (Group 1) maintains the current high rate of pelvic R0 resection and is consistent with non-inferiority for time to local recurrence (TLR).
  2. Phase III component: To compare neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) to standard 5FUCMT (Group 2) with respect to the primary endpoint of the Disease-Free Survival (DFS).
  Secondary
  1. To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard group 5FUCMT (Group 2) with respect to the proportion of patients who achieve a pathologic complete response (pCR) at the time of surgical resection.
  2. To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard 5FUCMT (Group 2) with respect to overall survival.
  3. To evaluate and compare the adverse event profile and surgery complications between two groups.
  4. To estimate the proportion of patients in the selective group (Group 1) who receive: 1) pre-operative 5FUCMT; 2) post-operative 5FUCMT; 3) either pre- or post-operative 5FUCMT.
  5. To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard 5FUCMT (Group 2) with respect to Local Recurrence (TLR)
  6. To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard 5FUCMT (Group 2) with respect to

Neoadjuvant Response Score (NAR)

Event monitoring of patients will continue up to 8 years post randomization.

Study Milestones:

Start date: June 12, 2012

Primary Completion Date: December 31, 2022

Publication Information:

Analysis Type: Primary

PubMed ID: 37272534

Citation: Schrag D, Shi Q, Weiser MR, Gollub MJ, Saltz LB, Musher BL. New England Journal of Medicine. 2023;389(4):322-334, doi: 10.1056/NEJMoa2303269.

Associated Datasets: NCT01515787-D1-Dataset.csv (final), NCT01515787-D2-Dataset.csv (ae)

Dataset Information:

Dataset Name: NCT01515787-D2-Dataset.csv (ae)

Description: Dataset NCT01515787-D2-Dataset.csv (ae) is one of 2 datasets associated with PubMed ID 37272534. This dataset contains data presented in the primary manuscript results section and supplementary Table 2A and Table 2B.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing, except where otherwise noted.

NCT01515787-D2-Dataset.csv (ae) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Adverse Event Grade	grade	1, 2, 3, 4, 5	
System Organ Class	soc		
De-identified ID	deid		
Pre vs Post Operative	prepost	Post-Operative, Pre-Operative	
Toxicity	toxicity		