ISRCTN11812525 https://doi.org/10.1186/ISRCTN11812525

Preoperative chemoradiation with UFT-E plue leucovorin and translational study for locally advanced rectal cancer

Submission date 05/07/2016	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 25/07/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 20/10/2017	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Rectal cancer is a type of cancer that develops in the large bowel. I'ts called rectal cancer because of its position within the length of the bowel. Patients that have been diagnosed with locally advanced rectal cancer (that is, cancer that has grown through the wall of the rectum but not yet spread to the lymph nodes) are often treated with both chemotherapy and radiation (chemoradiation) before they considered for surgery. This study is investigating the success of a particular treatment; namely a high-dose of a drug called tegafur-uracil together with another one called leucovorin in addition to radiation therapy for patients before they undergo surgery for locally advanced rectal cancer.

Who can participate?
Adults with locally advanced rectal cancer that have not yet been treated with chemotherapy.

What does the study involve?
All participants are given radiotherapy plus chemotherapy treatment with tegafur-uracil (400mg /m2/day) and leucovorin (90mg/day). The drugs are given to each patient throughout their radiation treatment. All participants are then followed up to see whether their cancer has responded to the treatment, whether they suffered any ill effects from the treatment, how long it is before the cancer reoccurs. Overall survival rate data is also collected. Participants are also asked to give blood samples for pharmacogenetic analysis to see whether people with certain genetic profiles are more likely to be successfully treated than others.

What are the possible benefits and risks of participating?
Participants are given the treatment without change for the duration of the study. There could be some adverse effects from taking the high dose of tegafur-uracil.

Where is the study run from?
National Cancer Center, Goyang (South Korea)

When is the study starting and how long is it expected to run for?
October 2008 to November 2012

Who is funding the study?
National Cancer Center, Goyang (South Korea)

Who is the main contact?
Ms Hyun Mi Kim
ncccolonco@hanmail.net

Contact information

Type(s)
Scientific

Contact name
Ms Hyun Mi Kim

Contact details
323 Ilsan-ro, Ilsandong-gu
Goyang
Korea, South
10408
82-31-920-1145
ncccolonco@hanmail.net

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NCC-CTS-08-358

Study information

Scientific Title
A phase II study of preoperative chemoradiation with UFT-E plus leucovorin and the translational research for detection of predictive markers in the patients with locally advanced resectable rectal cancer

Study objectives
Pathologic complete response rate with enteric coated tegafur-uracil(UFT-E) and leucovorin for locally advanced rectal cancer (cT3-4NxM0) would be more than 20%

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Boards of National Cancer Center, Korea, 20/10/2008, ref: NCCCTS-08-358

Study design
Single-arm phase II study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Locally advanced rectal cancer (cT3-4, Nx, M0)

Interventions
This is a single-arm, phase II study of preoperative radiotherapy (RT) with enteric-coated tegafur-uracil (UFT-E) and leucovorin.
1. Radiotherapy (RT): started within 14 days after screening and obtaining informed consent. RT to whole pelvis at a dose of 45 Gy in 25 fractions, followed by 5.4 Gy in a three-fraction boost to the primary tumor.
2. Enteric-coated tegafur-uracil (UFT-E) : 400 mg/m2 of tegafur divided into three daily doses without drug holidays during RT. - Since each package of UFT-E contains 500 mg of granules that correspons to 100 mg of tegafur, the recommended dosing schedule according to body surface area (BSA) are as follows:
2.1. BSA ≤ 1.37 m2: 2, 2, and 1 packages an hour after breakfast, lunch and dinner, respectively
2.2. BSA 1.38 m2 – 1.62 m2: 2, 2, and 2 packages; BSA 1.63 m2 – 1.87 m2: 3, 2, and 2 packages
2.3. BSA ³ 1.88 m2: 3, 3, and 2 packages
3. Leucovorin: 30mg (2 tablets) p.o. With each UFF-E dose, corresponding to a total daily dose of 90 mg
4. Surgery: planned within 6 ± 2 weeks of the completion of RT. Total mesorectal excision is the first-choice surgical treatment

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
1. Enteric-coated tefagur-uracil 2. Leucovorin

Primary outcome measure
Pathologic complete response by Dworak's classification, assessed with surgical specimen (including primary tumor and regional lymph nodes) derived from total mesorectal excision.

Dworak's classification:
Grade 0 no regression
Grade 1 dominant tumor mass with obvious fibrosis and/or vasculopathy Grade 2 dominantly fibrotic changes with few tumor cells or groups (easy to find)
Grade 3 very few (difficult to find microscopically) tumor cells in fibrotic tissue with or without mucous substance
Grade 4 no tumor cells, only fibrotic mass (total regression or response)

Secondary outcome measures
1. Safety: measured with National Cancer Institute Common Terminology Criteria (NCI-CTC) scale, version 3.0
2. Relapse-free survival : the time from the date of starting CRT to the date on which either of recurrence, progression, or death was first observed, or the date of last follow-up
3. Overall survival: the time from the date of starting CRT to the date of death from any cause or last follow-up
4. Pharmacogenetic analysis: genomic DNA from peripheral blood will be analyzed for the following polymorphism: CYP2A6*4 (whole deletion of CYP2A6), CYP2A6*7 (6558T>G, rs5031016), CYP2A6*9 (-48T>G, rs28399433), CYP2A6*10 (6558T>C and 6600G>T, rs28399468), UMPS 638G>C (rs1801019), ABCB1 3545 C>T (rs1045642), ABCB1 1236 C>T (rs1128503), and ABCB1 2677 G>T/A (rs2032582)

Overall study start date
20/10/2008

Completion date
30/11/2012

Eligibility

Key inclusion criteria
1. Histologically diagnosed adenocarcinoma of rectum
2. Located within 8cm from anal verge
3. cT3/4 by rectal MRI+/- endorectal ultrasound
4. 18 years old or more
5. ECOG performance status <=2
6. No previous chemotherapy
7. No previous radiotherapy to pelvis
8. Adequate bone marrow, hepatic, and renal function

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
121

Key exclusion criteria
1. Rectal cancer of histology other than adenocarcinoma
2. Adenocarcinoma developed from inflammatory bowel disease
3. Presence of distant metastases
4. Existence of unresected synchronous colon cancer
5. Unresolved bowel obstruction
6. Clinically unresectable disease
7. Uncontrolled cardiovascular disease
8. Uncontrolled active infection
9. History of other malignancies within 5 years from screening
10. History of organ transplantation that necessitates immunosuppressive treatment
11. Uncontrolled epileptic disease or psychiatric disease
12. Pregnant or breastfeeding women, or women with child-bearing potential who are not compliant to 13. Contraception policy of this study

Date of first enrolment
09/01/2009

Date of final enrolment
28/08/2012

Locations

Countries of recruitment
Korea, South

Study participating centre
National Cancer Center
323 Ilsan=ro, Ilsandong-gu
Goyang
Korea, South
10408

Sponsor information

Organisation
National Cancer Center

Sponsor details
323 Ilsan-ro, Ilsandong-gu
Goyang
Korea, South
10408

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02tsanh21

Funder(s)

Funder type
Not defined

Funder Name
National Cancer Center

Alternative Name(s)
NCC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Korea, South

Results and Publications

Publication and dissemination plan

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	27/03/2017		Yes	No