

ARISTOTLE: a phase III trial comparing standard versus novel chemoradiation treatment (CRT) as pre-operative treatment for magnetic resonance imaging (MRI)-defined locally advanced rectal cancer

Submission date 28/10/2008	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 08/09/2009	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 03/10/2023	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

<http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-standard-treatment-with-without-irinotecan-cancer-rectum-aristotle>

Study website

<http://www.ctc.ucl.ac.uk/TrialDetails.aspx?Trial=82&TherA=7>

Contact information

Type(s)

Public

Contact name

Ms Rubina Begum

Contact details

Cancer Research UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London
United Kingdom
W1T 4TJ
020 7679 9514
ctc.aristotle@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number

2008-005782-59

IRAS number**ClinicalTrials.gov number****Secondary identifying numbers**

Version 6.1

Study information

Scientific Title

ARISTOTLE: Advanced Rectal study with Standard Therapy Or a novel agent, Total mesorectal excision (TME) and Long term Evaluation

Acronym

ARISTOTLE

Study objectives

Some patients with rectal cancer benefit from receiving chemotherapy and radiotherapy before they have an operation to remove their cancers. This trial will determine whether the addition of a second drug (irinotecan) to the standard treatment of oral chemotherapy using capecitabine and radiotherapy will result in fewer cancer recurrences (regrowth) after the operation and if patients live longer.

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee London - Riverside, 17/09/2010, ref. 10/H0706/65

Study design

Two-arm phase III multicentre randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Locally advanced rectal cancer

Interventions

Current interventions (as of 15/01/2018):

Arm A: capecitabine 900 mg/m² orally twice daily Monday to Friday for five weeks with radiotherapy 45 Gy in 25 fractions.

Arm B: irinotecan 60 mg/m² intravenously (IV) once weekly, weeks 1 - 4 and capecitabine 650 mg/m² orally twice daily Monday to Friday for five weeks with radiotherapy 45 Gy in 25 fractions.

All patients will be followed up for 5 years after completion of chemoradiotherapy.

Previous interventions

Arm A: capecitabine 900 mg/m² orally twice daily Monday to Friday for five weeks with radiotherapy 45 Gy in 25 fractions.

Arm B: irinotecan 60 mg/m² intravenously (IV) once weekly, weeks 1 - 4 and capecitabine 650 mg/m² orally twice daily Monday to Friday for five weeks with radiotherapy 45 Gy in 25 fractions.

All patients will be followed up for 5 years.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Irinotecan, capecitabine

Primary outcome measure

Current primary outcome measures (as of 15/01/2018):

Disease free survival at 3 years after completion of chemoradiotherapy

Previous primary outcome measures as of 01/06/2016:

Disease free survival at 3 years

Previous primary outcome measures:

Disease free survival, assessed at four planned stages during the trial

Secondary outcome measures

Current secondary outcome measures (as of 15/01/2018):

1. Disease-specific survival
2. Loco-regional failure
3. Overall survival
4. Histopathologically confirmed circumferential resection margin (CRM) negative resection rate
5. Histopathological complete response pathological complete response (pCR) rate
6. Histopathologically quantitated tumour cell density
7. Surgical morbidity
8. Health-related Quality of Life (QoL) and functional outcome

9. Frequency and severity of adverse events
10. Compliance to trial treatment (radiotherapy, capecitabine and irinotecan)

Assessments weekly during treatment phase, then 1 and 4 weeks after completion of treatment, and then 4 - 6 weeks after completion of treatment.

Previous secondary outcome measures as of 01/06/2016:

1. Disease-specific survival
2. Loco-regional failure
3. Overall survival
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8. Health-related Quality of Life (QoL) and functional outcome

Previous secondary outcome measures:

1. Disease-specific survival
2. Loco-regional failure
3. Overall survival
4. Histopathologically confirmed circumferential resection margin (CRM) negative resection rate
5. Histopathological complete response pathological complete response (pCR)
6. Surgical morbidity
7. Functional outcome
8. Quality of life
9. Resource use

Assessments weekly during treatment phase and then at 2 and 4 weeks after completion of treatment, and then 4 - 6 weeks after completion of treatment.

Overall study start date

22/09/2011

Completion date

29/12/2023

Eligibility

Key inclusion criteria

Current inclusion criteria as of 01/06/2016:

1. Diagnosis of primary rectal cancer
2. Histologically confirmed invasive adenocarcinoma
3. Pelvic MRI defined disease (one of the following):
 - 3.1. Mesorectal fascia involved or breached
 - 3.1.1. Includes involvement of adjacent organ
 - 3.2. Mesorectal fascia threatened (tumour ≤ 1 mm from mesorectal fascia) includes:
 - 3.2.1. Primary tumour ≤ 1 mm from mesorectal fascia or
 - 3.2.2. Extra-mural vascular invasion ≤ 1 mm from mesorectal fascia or
 - 3.2.3. Tumour deposit with irregular border and mixed signal intensity ≤ 1 mm from mesorectal fascia
 - 3.3. Low tumours at/below level of levators where:

- 3.3.1. Tumour ≤ 1 mm from levator on two imaging planes or
- 3.3.2. Tumour through full thickness of muscularis propria or beyond at level of puborectalis sling or below or
- 3.3.3. Tumour involving the intersphincteric plane or
- 3.3.4. Tumour involving the external anal sphincter
- 3.3.5. Patients with enlarged pelvic side wall nodes are eligible only if they also meet at least one of the above criteria.
- 4. Superior extent of macroscopic tumour no higher than S1/2 junction on sagittal MRI
- 5. ECOG performance status 0 or 1
- 6. Considered fit to receive all trial treatments
- 7. Bowel function controlled with ≤ 6 mg loperamide per day
- 8. Absolute neutrophil count $> 1.5 \times 10^9/L$; platelets $> 100 \times 10^9/L$
- 9. Serum transaminase $< 3 \times$ ULN
- 10. Adequate renal function (Cockcroft-Gault estimation ≥ 50 mL/min)
- 11. Bilirubin $< 1.5 \times$ ULN
- 12. Able to swallow oral medication
- 13. Willing and able to give informed consent and comply with treatment and follow-up schedule
- 14. Aged 18 or over

Previous inclusion criteria:

- 1. Mesorectal fascia involved
- 2. Mesorectal fascia threatened (tumour less than 1 mm from mesorectal fascia)
- 3. Low tumours arising less than 5 cm from the anal verge
- 4. Patients aged 18 years and over, both male and female patients

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

600

Key exclusion criteria

Current exclusion criteria as of 01/06/2016:

- 1. Previous radiotherapy to the pelvis (including brachytherapy)
- 2. Uncontrolled cardiorespiratory comorbidity (includes patients with inadequately controlled angina or myocardial infarction within 6 months prior to randomisation)
- 3. Unequivocal evidence of metastatic disease (includes resectable metastases)
- 3.1. Patients with equivocal lesions (determined at MDT) are eligible
- 4. Major disturbance of bowel function (e.g. gross faecal incontinence or requiring > 6 mg loperamide each day)
- 5. History of another malignancy within the last 5 years except successfully treated non-melanoma cancer of skin or carcinoma in situ of uterine cervix

6. Known dihydropyrimidine dehydrogenase (DPYD) deficiency
7. Known Gilberts disease (hyperbilirubinaemia)
8. Taking warfarin that cannot be discontinued at least 7 days prior to starting treatment
9. Taking phenytoin or sorivudine or its chemically related analogues, such as brivudine
10. Gastrointestinal disorder which would interfere with oral therapy and its bioavailability
11. Pregnant, lactating, or pre menopausal women not using adequate contraception
12. Oral St John's Wort therapy that cannot be discontinued at least 14 days prior to starting treatment
13. Unfit to receive any study treatment or subsequent surgical resection

Previous exclusion criteria:

1. Patients unable or unfit to receive all study treatment
2. World Health Organization (WHO) performance status greater than or equal to 2
3. Metastatic disease
4. Pregnant or lactating

Date of first enrolment

25/10/2011

Date of final enrolment

29/06/2018

Locations

Countries of recruitment

United Kingdom

Study participating centre

103 centres

United Kingdom

-

Sponsor information

Organisation

Cancer Research UK and UCL Cancer Trials Centre (UK)

Sponsor details

90 Tottenham Court Road

London

United Kingdom

W1T 4TJ

Sponsor type

Charity

Website

<http://www.ctc.ucl.ac.uk/>

ROR

<https://ror.org/054225q67>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK (CRUK) (UK) (ref: C19942/A10016)

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Planned publication in a high impact peer reviewed journal approximately 1 year after end of trial.

Intention to publish date

31/12/2024

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type Details

Date created	Date added	Peer reviewed?	Patient- facing?
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[HRA research
summary](#)

28/06
/2023

No

No

[Other
publications](#)

Modeling Acute Chemoradiotherapy (CRT) Diarrhea Severity Using
Automatically Contoured Small Bowel

01/10
/2023

03/10
/2023

Yes

No