ISRCTN15070952 https://doi.org/10.1186/ISRCTN15070952

Evaluating the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma

Submission date 04/12/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 16/12/2014	**Overall study status** Completed	
Last Edited 11/04/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-chemotherapy-after-surgery-for-small-bowel-cancer-ballad

Contact information

Type(s)
Public

Contact name
Mrs Sarah Bradley

Contact details
CRUK CTU Glasgow
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN
0141 301 7540
sarah.bradley@glasgow.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2013-003047-29

ClinicalTrials.gov (NCT)
NCT04257461

Protocol serial number
BALLAD 2013

Study information

Scientific Title
A trial to evaluate the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma

Acronym
BALLAD

Study objectives
Current study hypothesis as of 12/07/2019:
Adjuvant fluoropyrimidine chemotherapy results in an improved outcome (DFS and OS) over observation alone after potentially curative surgery for stage I, II, III and IV SBA2. Adjuvant fluoropyrimidine and oxaliplatin chemotherapy results in an improved outcome (DFS and OS) over fluropyrimidine alone after potentially curative surgery for stage I, II, III and IV small bowel adenocarcinoma

Previous study hypothesis:
Adjuvant fluoropyrimidine chemotherapy results in an improved outcome (DFS and OS) over observation alone after potentially curative surgery for stage I, II and III SBA2. Adjuvant fluoropyrimidine and oxaliplatin chemotherapy results in an improved outcome (DFS and OS) over fluropyrimidine alone after potentially curative surgery for stage I, II and III small bowel adenocarcinoma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland Research Ethics Service 1, 05/03/2015, ref: 15/WS/0011

Study design
Open-label randomised controlled multi-centre global trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Small bowel adenocarcinoma

Interventions
Group 1: Patients will be randomised between observation and chemotherapy. Those patients who draw the chemotherapy arm and who have consented to this can go on to be randomised into the group 2 question. This is to be encouraged as it will add significant value and improve efficiency of the trial.
Group 2: Patients will be randomised to receive therapy with a fluoropyrimidine regimen or combination therapy of fluoropyrimidine plus oxaliplatin. Investigators must specify the fluoropyrimidine regimen at the time of randomisation for each individual patient. Any accepted

institutional standard IV 5-FU/Folinic Acid regimen or oral capecitabine regimen may be used. The combination regimen is specified as oxaliplatin delivered as part of a standard institutional fluoropyrimidine combination regimen. Treatment will continue for up to 24 weeks

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
1. Capecitabine 2. 5-FU 3. Oxaliplatin

Primary outcome(s)
Disease free survival is the primary end point for the trial. This is defined at time from randomisation to the first occurrence of the following events:
1. Disease relapse (confirmed by imaging)
2. Incidence of a new primary (confirmed by imaging and histology/cytology)
3. Death from any cause
Patients who experience none of these events are censored at the last date known to be alive.

Key secondary outcome(s))
1. Overall survival: The patient's survival status is determined at each follow-up visit. After the mandated clinic visits survival status data will come from responsible cancer centres, cancer registries and national databases and include long-term passive follow-up data such as that collected through collaboration with the National Cancer Intelligence Network in the U.K.
2. Toxicity of chemotherapy: Toxicity will be assessed using CTCAE version 4.0. Only toxicities that are at least grade 2 will be recorded on the CRF
3. Quality of life: This is assessed using the EORTC QLQ-C30, EORTC QLQ-CR29 v2.1 and EQ-5D scales
Health Economics: Assess the cost-effectiveness of 24 weeks adjuvant chemotherapy in comparison to observation alone; and assess the cost-effectiveness of 24 weeks adjuvant 5FU /Capecitabine monotherapy compared to 5FU/Capecitabine plus Oxaliplatin. Outcomes will be reported as incremental cost per DFS and incremental cost per QALY. 4. Establishment of a central tissue bank for patients with SBA

Completion date
28/02/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 12/07/2019:
1. R0 resected stage I, II, III or IV SBA
2. No evidence of residual or metastatic disease at laparotomy or on CT/MRI imaging of chest, abdomen and pelvis
3. Patients must be registered and randomised within 14 weeks of surgery and commence chemotherapy within 16 weeks of surgery
4. ECOG Performance Status of 0 or 1
5. Absolute neutrophil account ≥ 1.5 x109/l
6. Platelet count ≥ 100 x 109/l

7. Haemoglobin ≥90 g/l (previous transfusion is allowed)
8. AST and ALT ≤ 2.5 x upper limit of normal (ULN). (At least one of ALT or AST MUST be performed)
9. Creatinine clearance > 50 ml/min (calculated by Cockcroft Gault or Wright equation) or measured by EDTA
10. Serum bilirubin ≤ 1.5 x ULN
11. Signed and dated informed consent indicating that the patient has been informed of all the pertinent aspects of the trial prior to enrolment
12. Age ≥ 16 years
13. Willingness and ability to comply with scheduled visits, treatment plans and laboratory tests and other trial procedures

Previous participant inclusion criteria:
1. R0 resected stage I, II or III SBA
2. No evidence of residual or metastatic disease at laparotomy or on CT/MRI imaging of chest, abdomen and pelvis
3. Patients must be registered and randomised within 12 weeks of surgery and commence chemotherapy within 14 weeks of surgery
4. ECOG Performance Status of 0 or 1
5. Absolute neutrophil account ≥ 1.5 x109/l
6. Platelet count ≥ 100 x 109/l
7. Haemoglobin ≥90 g/l (previous transfusion is allowed)
8. AST and ALT ≤ 2.5 x upper limit of normal (ULN). (At least one of ALT or AST MUST be performed)
9. Creatinine clearance > 50 ml/min (calculated by Cockcroft Gault or Wright equation) or measured by EDTA
10. Serum bilirubin ≤ 1.5 x ULN
11. Signed and dated informed consent indicating that the patient has been informed of all the pertinent aspects of the trial prior to enrolment
12. Age ≥ 16 years
13. Willingness and ability to comply with scheduled visits, treatment plans and laboratory tests and other trial procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
69

Key exclusion criteria
Current participant exclusion criteria as of 12/07/2019:
1. Non-adenocarcinoma histology of small bowel tumour which includes but is not confined to

lymphoma, GIST, carcinoid or other neuroendocrine tumour, squamous carcinoma, melanoma or sarcoma.
2. Adenocarcinoma arising in the appendix or colorectum
3. Previous neo-adjuvant chemo(radio)therapy for SBA
4. Clinically significant cardiovascular disease (i.e. active or < 12 months since cerebrovascular accident, myocardial infarction, unstable angina, New York Heart Association [NYHA] grade II or greater congestive heart failure, serious cardiac arrhythmia requiring medication, uncontrolled hypertension)
5. Pregnancy/lactation or of child bearing potential and not using medically approved contraception. (Postmenopausal women must have been amenorrhoeic for at least 12 months to be considered of non-childbearing potential)
6. Previous invasive or non-invasive malignancy except:
(i) Ductal Carcinoma in Situ (DCIS) of the breast where treatment consisted of resection alone, (ii) cervical carcinoma in situ where treatment consisted of resection alone, (iii) basal cell or squamous cell carcinoma where treatment consisted of resection alone or radiotherapy, (iv) superficial bladder carcinoma where treatments consisted of resection alone or with a single installation of intracescical chemotherapy or with BCG treatment, (v) other cancers where the patient has been disease-free for at least 3 years and treatment was with curative intent and (vi) other cancers wih very low potential for recurrence can be discussed with the CI or his approved representative through the Glasgow CRUK Clinical Trials Unit where eligibility will be considered on an individual basis
7. Known or suspected dihydropyrimidine dehydrogenase (DPD) deficiency
8. Known untreated coeliac disease (may be enrolled if diet controlled), untreated chronic inflammatory bowel disease or other cause of malabsorption or intestinal obstruction
9. Grade ≥ 2 peripheral neuropathy
10. Administration of any investigational drug within 28 days or 5 half-lives, whichever is longer, prior to receiving the first dose
of trial treatment.
11. Previous hypersensitivity to platinum salts
12. Patients with clinically significant, active infections, or any other serious medical condition in which chemotherapy is contraindicated will be excluded
13. Patients with untreated vitamin B12 deficiency are excluded from receiving folinic acid as part of their chemotherapy regimen. However, these patients may be eligible for treatment with capecitabine fluoropyrimidine therapy, where no folinic acid is administered as part of the treatment regimen
14. Patients with clinically significant sensorineural hearing impairment are excluded from receiving oxaliplatin but will be eligible for the fluoropyrimidine monotherapy provided as a clinician's choice for patients in group 1 randomised to either observation or chemotherapy
15. Any patient receiving treatment with brivudine, sorivudine and analogues

Previous participant exclusion criteria:
1. Non-adenocarcinoma histology of small bowel tumour which includes but is not confined to lymphoma, GIST, carcinoid or other neuroendocrine tumour, squamous carcinoma, melanoma or sarcoma
2. Previous neo-adjuvant chemo(radio)therapy for SBA
3. Clinically significant cardiovascular disease (i.e. active or < 12 months since cerebrovascular accident, myocardial infarction, unstable angina, New York Heart Association [NYHA] grade II or greater congestive heart failure, serious cardiac arrhythmia requiring medication, uncontrolled hypertension)
4. Pregnancy/lactation or of child bearing potential and not using medically approved contraception. (Postmenopausal women must have been amenorrhoeic for at least 12 months to be considered of non-childbearing potential)

5. Previous malignancy other than adequately treated in situ carcinoma of the uterine cervix or basal or squamous cell carcinoma of the skin, unless there has been a disease free interval of at least 3 years and treatment was with curative intent
6. Known or suspected dihydropyrimidine dehydrogenase (DPD) deficiency
7. Known untreated coeliac disease (may be enrolled if diet controlled), untreated chronic inflammatory bowel disease or other cause of malabsorption or intestinal obstruction
8. Grade ≥ 2 peripheral neuropathy
9. Administration of any investigational drug within 28 days or 5 half-lives, whichever is longer, prior to receiving the first dose of trial treatment
10. Previous hypersensitivity to platinum salts

Date of first enrolment
25/08/2015

Date of final enrolment
31/08/2022

Locations

Countries of recruitment
United Kingdom

Belgium

France

Japan

Study participating centre
Beatson West of Scotland Cancer Centre
United Kingdom
-

Sponsor information

Organisation
Greater Glasgow and Clyde Healthboard and University of Glasgow

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type

Not defined

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 6	16/07/2021	26/11/2021	No	No