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Short treatment with the drug cyclophosphamide in bowel cancer

Submission date 01/06/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 16/11/2023	**Overall study status** Ongoing	
Last Edited 04/03/2026	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-low-dose-cyclophosphamide-bowel-cancer-biccc

Background and study aims
Bowel cancer is one of the leading causes of cancer-related deaths worldwide. In the early stages of the disease, many patients can be cured with surgery. However, in the later stages, bowel cancer can return or progress even after surgery and chemotherapy. One potential way of preventing relapse is by making the patient's immune system better at detecting and destroying any cancer cells that might remain after treatment.

T cells are a type of white blood cell that play a key role in the immune system. They identify and destroy infected or cancerous cells in the body by recognising specific proteins found on the cells' surface. Previous studies showed that T cells can recognise proteins expressed by bowel cancer cells. We have also completed a small clinical trial which demonstrated how using the drug, cyclophosphamide at a low dose can kick-start the T cell response to cancer cells, prolonging the survival of patients with very advanced bowel cancer. At this low dose, cyclophosphamide was found to be very safe.

The BICCC trial aims to test whether giving a low dose of cyclophosphamide for 4 weeks to stage 2 - 4 bowel cancer patients who have completed surgery/chemotherapy can help prevent relapse. Since cyclophosphamide kick-starts T cell response to cancer cells, we believe that this response may allow some patient's immune system to destroy any remaining bowel cancer cells. Blood samples will be taken to study these anti-cancer responses in a small group of trial participants.

Who can participate?
Eligible patients will be approached in approximately 10 centres across the UK including Wales, England and Scotland (500 participants; 250 participants in each arm).

What does the study involve?
Patients will be randomly assigned to either receive the trial treatment (low-dose cyclophosphamide) or be monitored by their clinical team for 13 weeks. All recruited patients

will have 5 trial visits for monitoring and to receive tablets which they will take at home. Patients will be followed for three years, allowing us to measure if cyclophosphamide can prevent disease relapse.

What are the possible benefits and risks of participating?
Benefits:
We cannot guarantee that there will be any direct benefits to you if you choose to take part in the BICCC trial. Some studies have shown that patients who take part in clinical trials may have better outcomes overall and that hospitals which are active in clinical research have better patient care outcomes. Some people also find the additional appointments with medical staff helpful. It is hoped that treatment with low-dose cyclophosphamide may help slow down the relapse (growth) of any leftover cancer cells if they are present, but we cannot say for certain whether this will be the case for those allocated to receive it. Your participation will also provide information about the trial treatment and colorectal cancer that may change the way we treat patients in the future.
Risks:
1. Trial treatment related side-effects:
Cyclophosphamide (50mg twice a day) should not result in significant toxicities as confirmed in our clinical trial TaCTiCC, and studies carried out by other groups which have demonstrated its safety. At this low-dose, cyclophosphamide treatment is unlikely to cause suppression of immune responses. However, higher doses have been linked to immune suppression which can lead to serious infections. Patients with immunosuppression or severe infections will be excluded from the trial. Participation will be restricted for patients with severe impairment of bone marrow function, renal and hepatic failure. Patients' liver and renal function as well as blood count will be assessed during the trial screening process.
Cyclophosphamide has the potential to cause harm to the reproductive system as well as to unborn children. Female participants of childbearing potential will take pregnancy tests before the start of cyclophosphamide. All patients of childbearing potential will be required to use contraception as necessary through the treatment course and 12 months after treatment.
Good communication between patients and the local research team can help to ensure that patients are aware of any potential side effects. Participant information sheets will advise of the potential risks for the trial. Adverse events will be monitored by the trial team and reported to the relevant committees and regulatory bodies.

2. The inconvenience of additional hospital visits:
Patients will need to attend 5 additional hospital visits to receive their tablets, have their health and side effects monitored and provide blood samples. Patients from Swansea, Bath and Bristol will be offered the opportunity to travel to Cardiff for their trial treatment/monitoring. This will give this subset of patients (~100 local to Cardiff) the chance to participate in the optional translational immune response analysis (secondary and tertiary endpoint). This is essential as the blood samples need to be analysed rapidly. It will be communicated to these patients that this an optional part of the trial. This subset of patients will be reimbursed for their travel.
Patients in the active monitoring arm will be offered 2 telephone follow-up appointments at the discretion of the PI.

3. Keeping track of medication schedules and symptoms: Patients will be required to self-administer their medication twice a day and asked to keep a diary to log their symptoms, which can be time-consuming and difficult to remember. Local research team will explain the process of self-administration to the participants, and hand out, explain and review patient diaries to ensure patients understand their medication schedules and the process of logging symptoms.

4. The risks of blood collection:
Blood tests are considered safe with very minimal risks. Possible adverse events of blood collection are tenderness/pain (mild and short-lived), bleeding/bruising, or feeling faint. Trained staff will perform the blood collection procedures using routine standard practices which address all the highlighted risks and ensure patient wellbeing at all times.

5. Risk of breach of confidentiality:
All recruited patients will be assigned a unique patient identification number. All trial data will be stored under the provisions of GDPR 2018. Any clinical information that leaves the hospital will have names and addresses removed to prevent participant identification.

6. Risk of participants misunderstanding the trial:
The trial will be clearly explained to all participants using the information sheet which has been reviewed by a patient representative. The patient information sheet and consent form will be provided in English (and Welsh on request).

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
May 2023 to September 2030

Who is funding the study?
Cancer Research Wales (UK)

Who is the main contact?
Dr Nicola Heady, biccc@swansea.ac.uk

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003780-10

Integrated Research Application System (IRAS)
1004377

Protocol serial number
SPON1890-22

Study information

Scientific Title
Brief intervention with cyclophosphamide in patients with colorectal cancer who completed treatment (BICCC)

Acronym
BICCC

Study objectives
Primary objective:
Measure the effect of oral low-dose cyclophosphamide on disease free survival in stage II - IVA colorectal cancer patients who have finished standard treatment. Disease free survival will be measured after 3 years because relapse occurs in 1:4 patients during this time.

Secondary objectives:
1. Assess the feasibility and tolerability of cyclophosphamide in this patient group.
2. Assess the effect of the cyclophosphamide on tumour-specific immune responses.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/09/2023, Fulham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8286; fulham.rec@hra.nhs.uk), ref: 23/LO/0538

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Stage II-IVA diagnosed colorectal cancer

Interventions
Intervention: Randomised, open-label, 2-arm study (with survival, safety and efficacy outcomes).

Total number of participants: 500

Randomisation scheme: Participants will be randomised 1:1 and stratified on disease stage (MSI high included) as well as block randomised. Randomisation list will be developed in consultation with Sealed Envelope Ltd (https://sealedenvelope.com).

Treatment duration: 9 weeks
Trial duration: 13 weeks
Follow up duration: 36 months post-randomisation by consulting secondary care patient notes /contacting treating clinician.

Trial arms:
Group 1 (Control/Active Monitoring Group) will receive standard of care which is no additional treatment or medication. Participants will be invited to attend 5 additional hospital visits (weeks 1, 4, 7, 10 and 13) for monitoring.

Group 2 (Trial Treatment/Cyclophosphamide Group) will receive oral low-dose cyclophosphamide tablets (50mg bd) in weeks 1, 3, 7 and 9. Participants will be invited to attend 5 additional hospital visits (weeks 1, 4, 7, 10 and 13) for monitoring.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cyclophosphamide

Primary outcome(s)
Disease free survival over 36 months from randomisation. Patients undergo standard clinical follow-up including at least two CT scans and six monthly serum CEA measurements (as recommended by NICE guideline on Colorectal cancer NG151). Disease recurrence or cancer-related death will be deemed an event. Recurrence will be evaluated at standard care appointments (timepoints depending on local site procedures) where potential disease relapse will be investigated by CT scan or other measures. Patient notes or discussion with patients' doctor will be used to determine disease free survival 3 years post-randomisation.

Key secondary outcome(s)
1. Toxicity as measured by CTCAE over the course of treatment and up to 4 weeks after the last dose of cyclophosphamide. Toxicity will be monitored via blood tests during the week 4 visit (after the first cycle) for the first 50 participants receiving the IMP (cyclophosphamide). Treatment will be stopped should 15% of Grade 3/4 toxicity events be experienced at any stage and no further participants will be recruited, otherwise recruitment will continue.
Adverse event reporting will be performed at weeks 4, 7, 10 and 13 for all patients.
2. Immunological responses defined as ≥2-fold increase in anti-5T4 IFN-γ+ T cell response at treatment day 22 v 1 and/or treatment day 64 v 43. Immune responses will be evaluated at baseline (week 1), during treatment (weeks 4 and 7) and post-treatment (weeks 10 and 13) in ~100 patients (local to Cardiff). Translational analysis will be performed after 25 and 50 participants are recruited to each group i.e. active monitoring group vs cyclophosphamide group.

Completion date
03/09/2030

Eligibility

Key inclusion criteria
1. Ability and willingness to provide written informed consent
2. Willing and able to comply with the trial visits and undergo treatment as scheduled
3. Age ≥ 50 years
4. Clinical diagnosis of colorectal cancer stage II – IVA
5. Completed treatment by surgery ± adjuvant chemotherapy and deemed ‘cured’
6. For participants receiving adjuvant chemotherapy:
6.1. Last dose of chemotherapy must be completed ≥ 4 weeks prior to first dose of trial therapy
6.2. First trial therapy dose must be started ≤ 4 months from last chemotherapy dose
7. For participants not receiving adjuvant chemotherapy surgery must be ≥ 6 weeks prior to first dose of trial therapy
8. WHO performance status 0 – 2
9. Female participants of childbearing potential (i.e. aged 50-55 in this study and not reached the menopause (postmenopausal state is defined as no menses for 12 months without an

alternative medical cause)) have a negative urine pregnancy test and are not breastfeeding
10. Female participants of childbearing potential and male participants with a female partner of childbearing potential must agree to use appropriate methods of contraception (male condoms, ovulation-inhibiting hormonal contraception, intrauterine device (IUD), intrauterine hormone-releasing system (IUS) or abstinence) until 6 months following the date of their final dose of trial treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Creatinine level >1.5 Upper Limit of Normal (ULN)
2. Bilirubin level >1.5 ULN, Alkaline Phosphatase/Alanine Aminotransferase >2.5 ULN
3. Haemoglobin <90 g/L
4. Diagnosed as being immunosuppressed, receiving oral steroids (> prednisolone 10 mg daily) (nasal sprays and inhalers are permitted) or receiving other immunosuppressive therapy
5. Uncorrected urinary tract obstruction or active urinary tract infection
6. Participant has clinically active autoimmune disease requiring treatment to suppress autoinflammation
7. Known underlying inflammatory bowel disease that is considered to be the key aetiological agent in the development of the CRC
8. “Currently active” second malignancy, other than non-melanoma skin cancer and previously diagnosed prostate cancer which is stable clinically ≥ for more than 5 years with or without hormone treatment. (Participants are not considered to have a "currently active” malignancy if they have completed therapy ≥ more than 5 years previously and have no known evidence of residual or recurrent disease)
9. Evidence of significant clinical factor/s or laboratory finding which in the opinion of the investigating physician makes it undesirable for the patient to participate in the trial
10. No participant should have a serious or uncontrolled intercurrent infection or be HIV positive
11. A contra-indication to taking CPM:
11.1. Hypersensitivity to CPM, any of its metabolites, or to other components of the tablet
11.2. Acute infections
11.3. Bone-marrow aplasia

11.4. Acute urothelial toxicity from cytotoxic chemotherapy or radiation therapy
11.5. Pregnancy - participants of childbearing potential must agree to wait 6 months after stopping CPM before attempting to conceive a child.
12. Medications not permitted before, during and after the trial:
12.1. Anti-fungal drugs (4 weeks before/after or during trial treatment)
12.2. Anti-viral drugs (4 weeks before/after or during trial treatment)
12.3. Chemotherapy (4 weeks before/after trial treatment start)
12.4. Hormone therapy (4 weeks/after before and during trial treatment)
12.5. Adrenalin (4 weeks before/after and during trial treatment)
12.6. Immunosuppressive agents (4 weeks before/after and during trial treatment)

Date of first enrolment
13/09/2024

Date of final enrolment
12/03/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
Wales
CF14 4XW

Study participating centre
Velindre Cancer Centre
Velindre Road
Cardiff
Wales
CF14 2TL

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road

Glasgow
Scotland
G12 0YN

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
Manchester
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M20 4BX

Study participating centre
Churchill Hospital
Old Road
Headington
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OX3 7LE

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
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L7 8XP

Study participating centre
Lincoln County Hospital
Greetwell Road
Lincoln
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LN2 5QY

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Charity

Funder Name
Cancer Research Wales

Alternative Name(s)
Ymchwil Canser Cymru, CRW

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The BICCC research team are committed to ensuring that data generated from this trial is put to good use by the cancer and wider research communities. It is BICCC policy to consider data sharing upon request from qualified scientific and medical researchers all data generated from its research whilst safeguarding intellectual property, the privacy and confidentiality of participants. BICCC will not release trial data until the primary results have been published.

All publications will be deposited in the institutional repository on https://orca.cardiff.ac.uk in compliance with copyright and embargo periods. All BICCC data requests should be submitted for consideration to the supporting clinical trials unit via STU@swansea.ac.uk. Access to BICCC anonymised data may be granted following review and in accordance with the BICCC Publication Policy.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes