ISRCTN40245896 https://doi.org/10.1186/ISRCTN40245896

A Phase II trial to find the durable clinical benefit of nivolumab in class II expressing microsatellite colorectal cancer

Submission date 01/04/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 04/04/2019	**Overall study status** Completed	
Last Edited 20/03/2026	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-nivolumab-for-advanced-bowel-cancer-anicca-class-ii

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03981146

Clinical Trials Information System (CTIS)
2018-000318-39

Integrated Research Application System (IRAS)
237804

Central Portfolio Management System (CPMS)
37422

Study information

Scientific Title
A phase II trial assessing nivolumab in class II expressing microsatellite stable colorectal cancer

Acronym
ANICCA-Class II

Study objectives
The primary objective of this trial is to detect the rate of durable clinical benefit in patients with class II expressing microsatellite stable colorectal cancer treated with single-agent nivolumab, to justify further investigation in subsequent studies.

The secondary objectives will be to evaluate the benefit to patients in terms of other clinical outcomes, to include:
1. Objective response rate
2. Best percentage change in sum of target lesion diameters
3. Time to maximal response
4. Progression-free survival time
5. Overall survival time

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/06/2019, South Central – Oxford B Research Ethics Committee (Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)20 7104 8049; nrescommittee.southcentral-oxfordb@nhs.net), ref: 19/SC/0107

Study design
Non-randomized; Interventional; Design type: Treatment, Screening, Immunotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
Informed consent:
Patients potentially suitable for the trial will be identified at an oncology clinic, and will be approached about the trial with the aid of the patient information sheet. After discussion about the trial and sufficient time to consider whether they wish to take part (usually at least 24 hours), the patient will be asked to sign an informed consent form in the presence of the research doctor. They will initially be provided with an information sheet explaining the purpose of the biopsy screening assessment and provide consent for this to be done. If MSS CRC with class II levels are demonstrated they will then be provided with the information sheet for the main trial and provide further consent to take part.

Screening investigations:
Following the informed consent process, the patient will undergo screening assessments. These will include:
Full medical history - To include smoking and alcohol history, any relevant significant medical conditions (other than colorectal cancer) and autoimmune conditions, history of treatment for the primary diagnosis, including prior systemic treatment, radiation treatment and surgical treatment including best response to prior treatments where applicable.
Date of last prior cancer treatment must be documented. Radiographic studies performed prior to trial entry may also be requested for review.
1. Coagulation parameters: Prothrombin (PT) / International Normalised Ratio (INR) and partial thromboplastin (aPTT)
2. CT scan with contrast – chest, abdomen and pelvis within 28 days of planned treatment date (RECIST v1.1 reporting).
3. Hepatitis C Virus (HCV) RNA (qualitative), Hepatitis B Surface Antigen and Human Immunodeficiency Virus (HIV) 1 / 2 antibodies.

The following screening tests should be undertaken locally up to 7 days prior to trial registration:
1. Physical examination including height and weight
2. Vital signs - temperature, pulse, respiratory rate and blood pressure (average of 3 BP readings)
3. ECOG performance status

4. Adverse events - Adverse Events (AEs) and laboratory safety measurements will be graded per NCI Common Terminology Criteria for Adverse Events (CTCAE) version v4.03 . All adverse events, whether gradable by CTCAE or not, will also be evaluated for seriousness
5. Concomitant medications – taken within four weeks prior to registration.
6. Full blood count (FBC) to include: white blood cells, haematocrit, haemoglobin, platelets, neutrophils, lymphocytes, red blood cells, monocytes, basophils, eosinophils, absolute neutrophil count
7. Urinalysis
8. Pregnancy test if applicable (urine or serum β-HCG)
9. Comprehensive serum chemistry panel to include: sodium, potassium, urea, nitrogen, creatinine, magnesium, calcium (total), bilirubin (total), direct bilirubin, albumin, alkaline phosphatase (ALP), aspartate transferase (AST), alanine transferase (ALT), glucose, lactate dehydrogenase (LDH), phosphate, total protein, C reactive protein (CRP), Carcinoembryonic antigen (CEA)
10. Renal function - Patients must have adequate renal function as defined by Creatinine clearance <1.5 x ULN concurrent with creatinine clearance >50 ml/min (calculated as per institutional standard)
11. Thyroid function and cortisol - analysis of cortisol, T3, T4 and Thyroid Stimulating Hormone (TSH)

Up to 24 hours to first treatment:
1. Urine pregnancy test, if cannot be confirmed as negative a serum test will be required

Treatment:
Nivolumab will be administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a dose of 3 mg/kg on day 1 every 2 weeks. Patients will receive nivolumab for a maximum of 2 years and enter then enter the follow-up period.

Updated 05/08/2020:
Treatment:
Nivolumab will be administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a dose of 480 mg every 28 days (4 weeks). Patients will receive nivolumab for a maximum of 2 years and enter then enter the follow-up period.

Routine and safety tests:
1. Physical examination including vital signs and measure of ECOG performance status
2. Routine blood samples for the analysis of haematology, biochemistry, thyroid function and cortisol
3. A CT scan of the chest, pelvis and abdomen
4. Adverse event review
5. Concomitant medication review

Research procedures:
1. A DNA sample (at baseline only)
2. ctDNA blood samples (at baseline, every 8 weeks and end of treatment)
3. Cytokine/chemokine and proteomics blood samples (at baseline, every 8 weeks and end of treatment)

Treatment discontinuation:
When a patient completes (or discontinues early) trial therapy, they will undergo the same tests

performed throughout treatment at their end of treatment visit.
The timing of all investigations and sampling are detailed in the protocol and the relevant Patient Information Sheet.

Follow up:
A mandatory Safety Follow-Up Visit should be performed approximately 28 days after the last infusion of study medication, and include:
1. Physical examination including vital signs and measure of ECOG performance status
2. Routine blood samples for the analysis of haematology, biochemistry, thyroid function and cortisol
3. Renal function by calculation in the first instance, and measurement is permitted if required
4. Adverse event review
5. Concomitant medication review

For patients who begin another cancer therapy before 28 days after discontinuation of study therapy, the Safety Follow-Up Visit should occur prior to the patient receiving another cancer therapy.

Follow up data will be provided every 4 weeks up to 6 months post treatment discontinuation then every 12 weeks up to five years to obtain disease progression details (if patient discontinued for non-progression reasons), record treatment after progression and death date if applicable.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Durable clinical benefit (DCB) defined as the occurrence of complete response (CR), partial response (PR) or stable disease (SD) for 27 weeks or greater

Key secondary outcome(s))
1. Objective response: overall tumour burden assessed using RECIST version at CT scans every 9 weeks from trial entry up to 45 weeks, then every 12 weeks, until disease progression
2. Best percentage change in sum of target lesion diameters - at each evaluation, the longest diameters of all selected target lesions will be measured and summed and the percentage change from the baseline measurement will be calculated. The best percentage change is the one that reflects either the greatest decrease or the least increase over the whole period of assessment.
3. Time to maximal response, defined as the time from commencement of trial treatment to the date of CT scan that first records the best objective response as per RECIST
4. Progression-free survival time, defined as the time from commencement of trial treatment to the date of CT scan when progressive disease first recorded or date of death without previously recorded progression
5, Overall survival time, defined as the time from commencement of trial treatment to the date of death

Completion date
26/11/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 05/08/2020:
1. Histologically confirmed locally advanced or metastatic MSS CRC with class II expression (greater than 1% cancer cell positivity for class II expression on immunohistochemistry)
2. Eastern Cooperative Oncology Group (ECOG) performance status 0-2
3. Age >= 18 years
4. Patients must have completed all standard of care therapy that the treating oncologist deems appropriate. Trial treatment as first-line therapy is permitted if the patient has declined standard of care therapy
5. CT scan of chest, abdomen, pelvis within 28 days of registration demonstrating uni-dimensionally measurable disease as per RECIST version 1.1
6. Demonstrate adequate haematological function:
6.1. Platelet count > = 100 x 109 /L
6.2. Neutrophils > = 1.5 x 109/L
6.3. Haemoglobin > = 90 g/L
7. Demonstrate adequate hepatic function:
7.1. Serum bilirubin < = 1.5 x upper limit of normal (ULN)
7.2. Serum AST or ALT < = 2.5 x ULN or < 5 x ULN in the presence of liver metastases
8. Demonstrate adequate renal function:
8.1. Creatinine clearance < 1.5 times ULN and > 30ml/min (as per institutional standard)
9. Provision of signed and dated, written informed consent prior to any trial-specific procedures, sampling and analyses.
10. Negative pregnancy test (female patients of reproductive potential)
11. Patients must agree to the use of contraception

Previous inclusion criteria:
1. Histologically confirmed locally advanced or metastatic MSS CRC with strong class II expression (greater than 50% cancer cell positivity for class II expression on immunohistochemistry)
2. Eastern Cooperative Oncology Group (ECOG) performance status 0-2
3. Age > = 18 years
4. Patients must have completed all standard of care therapy that the treating oncologist deems appropriate. Trial treatment as first-line therapy is permitted if the patient has declined standard of care therapy
5. CT scan of chest, abdomen, pelvis within 28 days of registration demonstrating uni-dimensionally measurable disease as per RECIST version 1.1
6. Demonstrate adequate haematological function:
6.1. Platelet count > = 100 x 109 /L
6.2. Neutrophils > = 1.5 x 109/L
6.3. Haemoglobin > = 90 g/L
7. Demonstrate adequate hepatic function:
7.1. Serum bilirubin < = 1.5 x upper limit of normal (ULN)
7.2. Serum AST or ALT < = 2.5 x ULN or < 5 x ULN in the presence of liver metastases
8. Demonstrate adequate renal function:
8.1. Creatinine clearance < 1.5 times ULN and > 30ml/min (as per institutional standard)
9. Provision of signed and dated, written informed consent prior to any trial-specific procedures,

sampling and analyses.
10. Negative pregnancy test (female patients of reproductive potential)
11. Patients must agree to the use of contraception

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
35

Key exclusion criteria
1. Previous treatment with PD1/PDL1 inhibitors
2. Untreated symptomatic brain or leptomeningeal metastatic disease
3. Medical or psychiatric conditions compromising informed consent
4. Any medical condition which, in the opinion of the Investigator, would compromise the ability of the patient to participate in the trial or which would jeopardise compliance with the protocol
5. Administration of chemotherapy, radioactive or biological cancer therapy within 4 weeks prior to the first dose of trial therapy
6. Patient has not recovered to CTCAE grade 1 or better from the Adverse Event (AE) due to cancer therapeutics administered more than 4 weeks earlier
7. Active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment
8. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment. Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment
9. Patient has risk factors for bowel obstruction or bowel perforation (examples include but not limited to a history of acute diverticulitis, intra-abdominal abscess and abdominal carcinomatosis)
10. Patient has a known history of other malignancy, unless the patient has undergone potentially curative therapy with no evidence of that disease for 3 years
11. Has a history of non-infectious pneumonitis requiring steroids or has active pneumonitis or significantly reduced transfer coefficient (KCO)
12. Female patients that are either pregnant or breastfeeding

13. Male and female patients (of childbearing age) not willing to use adequate contraception
14. Patient previously had a severe hypersensitivity reaction to treatment with another monoclonal antibody
15. Patient is positive for Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies), active Hepatitis B (HBsAg reactive) or Hepatitis C (HCV RNA (qualitative) is detected); patients with negative Hepatitis C antibody testing may not need RNA testing
16. Known history of tuberculosis
17. Patient has an active infection requiring therapy
18. Has received a live vaccine within 30 days prior to the first dose of trial treatment
19. Patient is, at the time of signing informed consent, a regular user (including "recreational use") of any illicit drugs or had a recent history (within the last year) of substance abuse (including alcohol)

Date of first enrolment
28/08/2019

Date of final enrolment
06/09/2021

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Address Trust HQ
PO Box 9551
Queen Elizabeth Medical Centre
Edgbaston
Birmingham
England
B15 2TH

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road

Glasgow
Scotland
G12 0XH

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

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
England
NW1 2PG

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Trust Offices
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Belfast Health & Social Care Trust
Knockbracken Healthcare Park
Saintfield Road
Belfast
Northern Ireland
BT8 8BH

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road

London
England
SW3 6JJ

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Western General Hospital
Crewe Rd S
Edinburgh
Scotland
EH4 2XU

Study participating centre
Freemans Hospital
Freeman Rd
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Rd
Birkenhead

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CH63 4JY

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Bristol-Myers Squibb

Alternative Name(s)
Bristol-Myers Squibb Company, Bristol Myers Squibb, Bristol-Myers Company, BMS

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing plan as of 12/12/2023:
For ANICCA-Class II data, scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. Requests should be made by returning a completed Data Sharing Request Form and curriculum vitae of the lead applicant and statistician to newbusiness@trials.bham.ac.uk. The Data Sharing Request Form captures information on the specific requirements of the research, the statistical analysis plan, and the intended publication schedule. The request will be reviewed independently by the Cancer Research UK Clinical Trials

Unit (CRCTU) Directors at the University of Birmingham in discussion with the Chief Investigator, relevant Trial Management Group and independent Trial Steering Committee. In making their decision the Director's Committee will consider the scientific validity of the request, the qualifications of the Research Group, the views of the Chief Investigator, Trial Management Group and Trial Steering Committee, consent arrangements, the practicality of anonymizing the requested data and contractual obligations. Where the CRCTU Directors and appropriate Trial Committees are supportive of the request, and where not already obtained, consent for data transfer will be sought from the Sponsor of the trial before notifying the applicant of the outcome of their request. It is anticipated that applicants will be notified of a decision within 3 months of receipt of the original request.

Previous IPD sharing plan as of 07/12/2023 to 12/12/2023:
The datasets generated during and/or analysed during the current study are/will be available upon request.

Previous 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
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/12/2025	07/01/2026	Yes	No
Abstract results		13/09/2022	07/12/2023	No	No
HRA research summary			28/06/2023	No	No
Plain English results			04/02/2026	No	Yes
Protocol file	version 7.0	01/11/2021	07/01/2026	No	No
Statistical Analysis Plan	version 2.0	02/12/2021	07/01/2026	No	No
Study website		11/11/2025	11/11/2025	No	Yes