

# A trial assessing preoperative chemotherapy in patients with locally advanced but operable colon cancer

<b>Submission date</b> 24/05/2021	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 28/09/2021	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 05/09/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

After lung cancer, bowel (colorectal) cancer is the next most common cause of cancer death in the UK. Doctors usually treat bowel cancer with surgery often followed by chemotherapy to help stop the cancer from coming back. Despite all of the medical advances in recent years, until recently there have been no significant improvements to this treatment approach. However, an international research trial (FOxTROT 1) carried out in the UK, Denmark and Sweden, showed that having some chemotherapy (using the normal chemotherapy drugs for bowel cancer) before surgery (known as neoadjuvant chemotherapy), was safe and reduced the chances of the cancer coming back. However, patients in this study were mainly young and fit. Thanks to funding from Yorkshire Cancer Research, this important study will now be extended to see whether the same procedure is effective with gentler neoadjuvant chemotherapy before surgery in older patients or those with other medical problems (FOxTROT 2). This will be compared to the standard treatment of surgery first. FOxTROT 3 is a trial for younger, fitter patients. FOxTROT 4 (supported by Merck and Pierre Fabre) is a trial for people with a genetic mutation called BRAF. FOxTROT 5 (supported by GSK) is a trial for older patients or those with other medical problems whose tumour has an abnormality called deficient mismatch repair (dMMR).

### Who can participate?

Patients who are at least 18 years old and have locally advanced but operable colon (bowel) cancer. Patients who are older and less fit will be considered for FOxTROT 2 and FOxTROT 5. Patients who are younger and fitter will be considered for FOxTROT 3. Patients with a genetic mutation called BRAF may be considered for FOxTROT 4. The patient's oncologist will decide which trial the patient is suitable for.

### What does the study involve?

Patients will receive either the new approach (neoadjuvant treatment) or standard treatment. Patients allocated to the new approach will have neoadjuvant treatment (duration varies depending on the trial in which the patient is taking part) then a 3-to-4-week rest period. Then they will have an operation to remove the tumour. Patients allocated to standard treatment will

have their operation first. For all patients there will then be a 4-to-8-week recuperation period after surgery to allow for recovery. Depending on the trial the patient is recruited to, they will then be offered further trial treatment or transfer to standard care.

What are the possible benefits and risks of participating?

There is no guarantee that participants will benefit from the treatment given in this study. The chemotherapy given before surgery in FOxTROT 2 and FOxTROT 3 is the same as that given in standard care (just given before surgery, rather than after surgery). Patients may be more likely to have chemotherapy as part of their cancer treatment if given before surgery, rather than after surgery (current usual treatment). This was the case for patients in the FOxTROT 1 trial. FOxTROT 1 also showed that patients tended to have fewer complications after the operation if they had chemotherapy first.

There is a small risk that the tumour may continue to grow whilst receiving the treatment and the patient may need to have an emergency operation or stent. There is a risk of severe side effects from the treatment that may mean that the surgery is delayed, or that the patient may not be fit enough for an operation. However, the side effects of the chemotherapy given are well known and will be closely monitored by the medical team.

Where is the study run from?

Clinical Trials Research Unit (CTRU) at the University of Leeds (UK)

When is the study starting and how long is it expected to run for?

December 2020 to August 2029

Who is funding the study?

1. Yorkshire Cancer Research (UK)
2. Merck (Germany)
3. Pierre Fabre (France)
4. GSK (UK)

Who is the main contact?

Dr Lucy Bailey, FOxTROT@leeds.ac.uk

Mrs Claire Dimbleby, FOxTROT@leeds.ac.uk (FOxTROT 4)

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-chemotherapy-before-surgery-for-bowel-cancer-in-older-people-foxtrot-2>

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-comparing-2-combinations-of-chemotherapy-for-bowel-cancer-foxtrot-3>

## Contact information

### Type(s)

Public

### Contact name

Mrs Claire Dimbleby

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2021-002216-31

### Integrated Research Application System (IRAS)

1003812

### ClinicalTrials.gov (NCT)

NCT06293625

### Protocol serial number

MO21/126572, CPMS 49772, IRAS 1003812, CTRI/2023/07/055141 - India only

## Study information

### Scientific Title

FOxTROT: personalising neo-adjuvant chemotherapy in locally advanced but operable colon cancer

### Acronym

FOxTROT

### Study objectives

The overall aim of the FOxTROT trial platform is to refine and personalise the use of the neoadjuvant chemotherapy pathway in locally advanced operable colon cancer. As well as testing new clinical hypotheses within the platform, molecular stratification from diagnostic tissue will create future opportunities to test targeted novel agents with proven efficacy and safety in colon cancer.

FOxTROT 2: The alternative hypothesis is that the proportion of patients alive and disease-free at 3 years after randomisation treated with neoadjuvant chemotherapy (OxFp) is superior compared to those going straight to surgery. The null hypothesis is that there is no difference in the proportion of patients alive and disease-free at 3 years after randomisation.

FOxTROT 3: The alternative hypothesis is that the distribution of the tumour regression grade at the time of surgery allocated to mFOLFOXIRI is superior compared to those allocated to OxFp. The null hypothesis is that there is no difference in tumour regression grade (TRG).

(added 17/10/2023):

FOxTROT 4: The alternative hypothesis is that 6 weeks of neoadjuvant treatment with the EC doublet will be safe and result in significant tumour regression compared with 6 weeks of neoadjuvant oxaliplatin and fluoropyrimidine (OxFp) chemotherapy.

(added 14/08/2024)

FOxTROT 5: The alternative hypothesis is that in older and/or frail patients with untreated locally advanced dMMR/MSI-H CC, 12 weeks of neoadjuvant dostarlimab (an anti-PD1 monoclonal antibody) prior to surgery with curative intent, followed by 36 weeks of post-operative dostarlimab, will demonstrate similar efficacy to that seen in younger and fitter populations.

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 22/11/2021, Oxford-A Research Ethics Committee (Level 3, Block B, Whitefriars, Bristol, BS1 2NT, United Kingdom; +44 (0)207 1048206; oxforda.rec@hra.nhs.uk), ref: 21/SC/0277

### **Study design**

Stratified multi-arm multi-site randomized trial platform

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Locally advanced but operable colon cancer

### **Interventions**

Current interventions as of 14/08/2024:

FOxTROT is a stratified, multi-arm, multi-site randomised trial platform for patients with locally advanced but operable colon cancer. Prior to the initial registration period, all patients will have been assessed at a colon cancer MDT for review of pathology and radiology and potential participants will be identified. Patients meeting the registration eligibility criteria will be registered and a decision will be made about which FOxTROT comparison is most suitable. Participants will then be randomised in the appropriate comparison.

FOxTROT 2 randomises participants between two trial arms:

1. Straight to surgery: patients will proceed straight to surgery as soon as possible and will be assessed for adjuvant chemotherapy as standard care.
2. Neoadjuvant chemotherapy followed by surgery. Participants in this arm will receive 6 weeks of OxFP chemotherapy with a choice (non-randomised) between two regimens: OxMdG (2-weekly oxaliplatin/calcium folinate/infusional fluorouracil) or OxCap (3-weekly oxaliplatin with capecitabine). These should be delivered as per local practice. The clinician has two options of initial dosing as described above: full dose OxFp, or 80% dose OxFp. Treatment should start as soon as possible following randomisation. Patients should be reviewed prior to each cycle of treatment to assess for toxicity and any evidence of disease progression. Following the completion of neoadjuvant chemotherapy, all participants will be reviewed in the oncology clinic to be assessed for adjuvant chemotherapy.

FOxTROT 3 randomises participants between two trial arms:

1. In the control arm, Neoadjuvant chemotherapy (NAC) consists of 6 weeks of standard OxFp

with a choice (non-randomised) of either OxMdG (2-weekly oxaliplatin/calcium folinate /infusional fluorouracil) or OxCap (3-weekly oxaliplatin with capecitabine).

2. In the experimental arm, NAC comprises three 2-weekly cycles of mFOLFOXIRI (oxaliplatin, irinotecan, calcium folinate, then a 46-hour infusion of fluorouracil).

For both arms, treatment should start as soon as possible following randomisation. Patients will receive postoperative adjuvant chemotherapy (AC) of either 6 or 18 weeks, bringing the total NAC/AC duration to 3 or 6 months respectively. In the control arm, AC is with OxFp; in the experimental arm AC may be either mFOLFOXIRI or OxFp.

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2. In the experimental arm, Neoadjuvant systemic anti-cancer therapy (NA SACT) comprises three 2-week cycles of cetuximab and encorafenib once daily (EC). Treatment should start as soon as possible following randomisation. Postoperative adjuvant treatment will be as per local practice.

FOxTROT 5 is a single-arm study and all participants will receive 12 weeks (a maximum of four, 3-weekly cycles; 500 mg IV on day 1 of each cycle) of preoperative dostarlimab and 36 weeks (a maximum of six, 6-weekly cycles; 1000 mg IV on day 1 of each cycle) of postoperative dostarlimab. Treatment should start as soon as possible following enrolment.

Participants will be randomised or enrolled using a central automated 24-hour internet service based at the Leeds Clinical and Translational Research Unit (CTRU).

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2. Neoadjuvant chemotherapy followed by surgery. Participants in this arm will receive 6 weeks of OxFP chemotherapy with a choice (non-randomised) between two regimens: OxMdG (2-weekly oxaliplatin/calcium folinate/infusional fluorouracil) or OxCap (3-weekly oxaliplatin with capecitabine). These should be delivered as per local practice. The clinician has two options of initial dosing as described above: full dose OxFp, or 80% dose OxFp. Treatment should start as soon as possible following randomisation. Patients should be reviewed prior to each cycle of treatment to assess for toxicity and any evidence of disease progression.

Following the completion of neoadjuvant chemotherapy, all participants will be reviewed in the oncology clinic to be assessed for adjuvant chemotherapy.

Participants will be randomised using a central automated 24-hour internet service based at the Leeds Clinical and Translational Research Unit (CTRU).

## Intervention Type

Drug

## Phase

Phase II/III

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

FOxTROT 2: Oxaliplatin, calcium folinate, infusional fluorouracil, capecitabine; FOxTROT 3: Irinotecan, Oxaliplatin, calcium folinate, Fluorouracil, Capecitabine; FOxTROT 4: Oxaliplatin, calcium folinate, infusional fluorouracil, capecitabine, Cetuximab, Encorafenib; FOxTROT 5: Dostarlimab.

### Primary outcome(s)

FOxTROT 2: Disease-free survival (DFS), defined as the time from randomisation to disease recurrence, treatment failure, or death from any cause. The date of recurrence will be taken as the date of the CT scan which concluded disease recurrence. If a CT scan is not carried out, the date of recurrence will be taken as the date of the sample which indicated disease recurrence. Individuals who are lost to follow-up or are alive and disease-free at the time of analysis will be censored at their last date known to be alive and disease-free.

FOxTROT 3: Tumour regression grade (TRG) (categorised as no response, mild, moderate, marked and complete response), measured at the time of surgery according to the modified Dworak grading system. DFS will be defined as per the FOxTROT 2 primary endpoint.

(added 17/10/2023)

FOxTROT 4: Tumour regression grade (TRG) categorised as response or no response, measured at the time of surgery according to the modified Dworak grading system, where response includes the subcategories mild, moderate, marked and complete response.

(added 14/08/2024)

FOxTROT 5: Proportion of participants with a pathological complete response in the resected tumour following neoadjuvant dostarlimab.

### Key secondary outcome(s)

Current secondary outcome measures as of 14/08/2024:

Applicable to FOxTROT 2, FOxTROT 3, FOxTROT 4 and FOxTROT 5, where not part of the primary outcome measures:

1. Tumour regression grade (TRG) measured according to the modified Dworak grading system at the time of surgery
2. Tumour regression score (TRS) (categorised as poor/no response, partial, near complete and complete response), measured at the time of surgery
3. Histopathological endpoints, measured from pathological samples at the time of surgery:
  - 3.1. Tumour cell density
  - 3.2. Maximum tumour size
  - 3.3. Depth of invasion
  - 3.4. Apical node involvement
  - 3.5. Peritoneal involvement
  - 3.6. Nodal involvement
  - 3.7. R1/R2 resection rates
- 4 Short-term efficacy (and association with longer-term outcomes):
  - 4.1. Downstaging by T-stage, measured at pre-registration, post- neoadjuvant treatment (NAT) and 3-years post randomisation
  - 4.2. Minimal residual disease by ctDNA and ctDNA alterations during NAT measured from blood

- samples collected at baseline, prior to each cycle of NAT, post-NAT and prior to adjuvant therapy
5. Safety and toxicity (treatment related) defined as the adverse reactions (ARs or irARs) and serious adverse events (SAEs) (including serious adverse reactions (SARs) and serious unexpected serious adverse reactions (SUSARs)) reported on the trial according to CTCAE v5.0 and Clavien-Dindo.
  6. Cancer-related survival, defined as the time from randomisation to death caused by the same cancer, whether due to the original tumour or to a second primary same cancer. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive. Death not related to cancer will be specified as a competing risk.
  7. Overall survival, defined as the time from randomisation to death from any cause. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive.
  8. Surgical morbidity, defined as any surgery-related complication within 30 days post-surgery and surgical mortality, defined as death from any cause within 30 days post-surgery.
  9. Patient-reported outcomes (PROs) assessed according to outcomes measured on the EQ-5D5L and QLQ-C30 and CR29. PROs will be collected at timepoints defined according to the protocol.
  10. Geriatric assessment scoring, will be determined by the collection of domains used to assess frailty, full details of which are provided in the FOxTROT 2 protocol. Geriatric assessment data will be collected at baseline, and prior to adjuvant treatment – FOxTROT 2 and FOxTROT 5 only
  11. Disease-free survival (DFS)
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Previous secondary outcome measures as of 17/10/2023 to 14/08/2024:

1. Tumour regression grade (TRG) measured according to the modified Dworak grading system at the time of surgery – FOxTROT 2 only
2. Tumour regression score (TRS) (categorised as poor/no response, partial, near complete and complete response), measured at the time of surgery – FOxTROT 2, FOxTROT 3 & FOxTROT 4
3. Histopathological endpoints, measured from pathological samples at the time of surgery – FOxTROT 2, FOxTROT 3 & FOxTROT 4:
  - 3.1. Tumour cell density
  - 3.2. Maximum tumour size
  - 3.3. Depth of invasion
  - 3.4. Apical node involvement
  - 3.5. Peritoneal involvement
  - 3.6. Nodal involvement
  - 3.7. R1/R2 resection rates
4. Short-term efficacy (and association with longer-term outcomes) – FOxTROT 2, FOxTROT 3 and FOxTROT 4:
  - 4.1. Downstaging by T-stage, measured at pre-registration, post-NAC and 3-years postrandomisation
  - 4.2. Minimal residual disease by ctDNA and ctDNA alterations during neoadjuvant chemotherapy (NAC), measured from blood samples collected at baseline, prior to each cycle of NAC, post-NAC and prior to adjuvant chemotherapy
5. Safety and toxicity (both surgical and chemotherapy-related) defined as the adverse reactions (ARs) and serious adverse events (SAEs) (including serious adverse reactions (SARs) and serious unexpected serious adverse reactions (SUSARs)) reported on the trial according to CTCAE v5.0 and Clavien-Dindo – FOxTROT 2, 3 and 4
6. Cancer-related survival, defined as the time from randomisation to death caused by the same cancer, whether due to the original tumour or to a second primary same cancer. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive. Death not related to cancer will be specified as a competing risk – FOxTROT 2,

## FOxTROT 3 and FOxTROT 4

7. Overall survival, defined as the time from randomisation to death from any cause. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive – FOxTROT 2, FOxTROT 3 and FOxTROT 4
8. Surgical morbidity, defined as any surgery-related complication within 30 days post-surgery and surgical mortality, defined as death from any cause within 30 days post-surgery – FOxTROT 2, FOxTROT 3 and FOxTROT 4
9. Patient-reported outcomes (PROs) assessed according to outcomes measured on the EQ-5D5L and QLQ-C30 and CR29. PROs will be collected at baseline, post-NAC, prior to adjuvant chemotherapy, 12 months post-randomisation and 3 years post-randomisation – FOxTROT 2,
10. Geriatric assessment scoring, will be determined by the collection of domains used to assess frailty, full details of which are provided in the FOxTROT 2 protocol. Geriatric assessment data will be collected at baseline, and prior to adjuvant chemotherapy – FOxTROT 2 only
11. Disease-free survival (DFS) – FOxTROT 4

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## Previous secondary outcome measures:

1. Tumour regression grade (TRG) measured according to the modified Dworak grading system at the time of surgery – FOxTROT 2 only
2. Tumour regression score (TRS) (categorised as poor/no response, partial, near complete and complete response), measured at the time of surgery – FOxTROT 2&3
3. Histopathological endpoints, measured from pathological samples at the time of surgery – FOxTROT 2&3:
  - 3.1. Tumour cell density
  - 3.2. Maximum tumour size
  - 3.3. Depth of invasion
  - 3.4. Apical node involvement
  - 3.5. Peritoneal involvement
  - 3.6. Nodal involvement
  - 3.7. R1/R2 resection rates
4. Short-term efficacy (and association with longer-term outcomes) – FOxTROT 2 & 3:
  - 4.1. Downstaging by T-stage, measured at pre-registration, post-NAC and 3-years post-randomisation
  - 4.2. Minimal residual disease by ctDNA and ctDNA alterations during neoadjuvant chemotherapy (NAC), measured from blood samples collected at baseline, prior to each cycle of NAC, post-NAC and prior to adjuvant chemotherapy
5. Safety and toxicity (both surgical and chemotherapy-related) defined as the adverse reactions (ARs) and serious adverse events (SAEs) (including serious adverse reactions (SARs) and serious unexpected serious adverse reactions (SUSARs)) reported on the trial according to CTCAE v5.0 and Clavien-Dindo – FOxTROT 2 & 3
6. Cancer-related survival, defined as the time from randomisation to death caused by the same cancer, whether due to the original tumour or to a second primary same cancer. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive. Death not related to cancer will be specified as a competing risk – FOxTROT 2 & 3
7. Overall survival, defined as the time from randomisation to death from any cause. Individuals who are lost to follow-up or are still alive at the time of analysis will be censored at their last date known to be alive – FOxTROT 2 & 3
8. Surgical morbidity, defined as any surgery-related complication within 30 days post-surgery and surgical mortality, defined as death from any cause within 30 days post-surgery – FOxTROT

2 & 3

9. Patient-reported outcomes (PROs) assessed according to outcomes measured on the EQ-5D-5L and QLQ-C30 and CR29. PROs will be collected at baseline, post-NAC, prior to adjuvant chemotherapy, 12 months post-randomisation and 3 years post-randomisation – FOxTROT 2 & 3

10. Geriatric assessment scoring, will be determined by the collection of domains used to assess frailty, full details of which are provided in the FOxTROT 2 protocol. Geriatric assessment data will be collected at baseline, and prior to adjuvant chemotherapy – FOxTROT 2 only

## Completion date

01/08/2029

## Eligibility

### Key inclusion criteria

Current inclusion criteria as of 14/08/2024:

FOxTROT Registration Inclusion Criteria:

1. Biopsy-confirmed adenocarcinoma of the colon (or upper rectum if too high for radiotherapy); high-grade dysplasia is acceptable with unequivocal radiological evidence of invasive cancer\*
2. Radiological stage T3-4, N0-2, M0
3. Patient being treated with curative intent
4. Tumour tissue is available for molecular testing (local or central)
5. Age  $\geq 18$  years at the time of registration
6. Patient able and willing to provide written informed consent for the study

\* Patients with synchronous colonic tumours are eligible if the most advanced tumour meets the criteria above (please note MMR/MSI testing requirements for randomisation depending upon the location of the most advanced tumour)

FOxTROT 2 Inclusion Criteria:

1. Patients will be unsuitable for mFOLFOXIRI due to oncologist assessed frailty or comorbidity
2. Proficient mismatch repair (pMMR)/MSS tumour status for right sided tumours
3. Colorectal cancer (CRC) specialist-assessed fit to receive 6 weeks of NAC with OxFp (either full or modified dose) and surgery
4. Adequate full blood count: white blood cell (WBC)  $>3.0 \times 10^9/l$ ; platelets (PLTs)  $>100 \times 10^9/l$ .
5. Anaemia (Hb  $<10.0$  g/dl) is not an exclusion, but should be corrected by transfusion prior to
6. surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy can be given at the decision of the surgical and oncology teams.
7. Adequate renal biochemistry: glomerular filtration rate (GFR)  $>50$  ml/min as assessed by local standards
8. Adequate hepatobiliary function: bilirubin  $<1.5$  upper limit of normal (ULN) (patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study)
9. If female and of childbearing potential must agree to avoid pregnancy during and for 6 months after last dose of study treatment
10. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
11. Signed the Informed Consent Document for randomisation

FOxTROT 3 Inclusion Criteria:

1. Patients need to be fit and suitable for mFOLFOXIRI. There is no fixed age cut-off, but most patients will be under 70 years.

2. pMMR/MSS tumour status for right sided tumours
3. Adequate full blood count: WBC  $>3.0 \times 10^9/l$ ; Neutrophils  $\geq 1.5 \times 10^9/l$ ; Plts  $>100 \times 10^9/l$ . Anaemia (Hb  $< 100$  g/l) is not an exclusion, but should be corrected by transfusion prior to surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy can be given at the decision of the surgical and oncology teams.
4. Adequate renal biochemistry: glomerular filtration rate (GFR)  $>50$  ml/min as assessed by local standards
5. Adequate hepatobiliary function: bilirubin  $<1.5$  upper limit of normal (ULN) (patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study)
6. If female and of childbearing potential must agree to avoid pregnancy during and for 6 months after last dose of study treatment
7. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
8. Signed the Informed Consent Document for randomisation

FOXTROT 4 inclusion criteria:

1. pMMR/MSS colon adenocarcinoma (histologically confirmed).
2. Suitable for surgical resection and peri-operative SACT
3. No metastatic disease on routine staging investigations.
4. No prior treatment for bowel cancer
5. BRAFV600E mutation present in tumour biopsy (tested locally or centrally)
6. Adequate full blood count: WBC  $>3.0 \times 10^9/l$ ; Neutrophils  $\geq 1.5 \times 10^9/l$ ; Plts  $\geq 100 \times 10^9/l$ . Anaemia (Hb  $< 100$  g/l) is not an exclusion but should be corrected by transfusion prior to surgery and SACT. If Hb remains low despite transfusions, surgery and SACT can be given at the decision of the surgical and oncology teams.
7. Adequate renal biochemistry: GFR  $>50$  ml/min as assessed by local standards
8. Adequate hepatobiliary function: bilirubin  $< 1.5 \times$  ULN (Patients with Gilbert's syndrome who have raised bilirubin, but otherwise normal liver function tests are eligible for the study.) AST/ALT  $<2.5 \times$  ULN.
9. If female and of childbearing potential, must agree to avoid pregnancy during and for 6 months after the last dose of study treatment\*
10. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 6 months after the last dose of study treatment\*
11. Signed the Informed Consent Document for randomisation

FOXTROT 5 inclusion criteria:

1. Patients aged 70 years or more and/or with investigator-assessed frailty
2. dMMR and/or MSI-H tumour status by local or central assessment
3. Colon cancer specialist assessed fit to receive neoadjuvant dostarlimab and undergo surgery (refer to section 8.1 and Table 1 for guidance on assessing patient suitability for inclusion in FOXTROT 5)
4. Adequate full blood count: WBC  $>3.0 \times 10^9/l$ ; Platelets  $>100 \times 10^9/l$ ; neutrophils  $\geq 1.5 \times 10^9/l$ . Anaemia (Hb  $<9.0$  g/dl) is not an exclusion but should be corrected by transfusion prior to commencement of study treatment. If Hb remains low despite transfusions, surgery and immunotherapy can be given at the discretion of the surgical and oncology teams
5. Adequate renal biochemistry: GFR  $\geq 30$  ml/min/1.73m<sup>2</sup> for participants with serum creatinine (Cr)  $\geq 1.5 \times$  ULN OR Cr  $<1.5 \times$  ULN
6. Adequate hepatobiliary function: Bilirubin  $\leq 1.5 \times$  ULN (isolated bilirubin  $>1.5 \times$  ULN is acceptable if bilirubin is fractionated and direct bilirubin  $<35\%$ ) AST/ALT  $\leq 2.5 \times$  ULN

7. For participants not taking warfarin: INR <1.5 or PT <1.5 x ULN and either PTT or aPTT <1.5 x ULN. Participants taking warfarin may be included on a stable dose with a therapeutic INR <3.5
  8. If female and of childbearing potential, must agree to avoid pregnancy during and for 4 months after last dose of study treatment\*
  9. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 4 months after the last dose of study treatment\*
  10. Signed the Informed Consent Document for participation
- 

Previous inclusion criteria as of 17/10/2023 to 14/08/2024:

FOxTROT Registration Inclusion Criteria:

1. Biopsy-confirmed adenocarcinoma of the colon (or upper rectum if too high for radiotherapy); high-grade dysplasia is acceptable with unequivocal radiological evidence of invasive cancer\*
  2. Radiological stage T3-4, N0-2, M0
  3. Patient being treated with curative intent
  4. Tumour tissue is available for molecular testing (local or central)
  5. Age  $\geq 18$  years at the time of registration
  6. Patient able and willing to provide written informed consent for the study
- \* Patients with synchronous tumours are eligible if the most advanced tumour meets the criteria above (please note MMR/MSI testing requirements for randomisation depending upon the location of the most advanced tumour)

FOxTROT 2 Inclusion Criteria:

1. Patients will be unsuitable for mFOLFOXIRI due to oncologist assessed frailty or comorbidity
2. Proficient mismatch repair (pMMR)/MSS tumour status for right sided tumours
3. Colorectal cancer (CRC) specialist-assessed fit to receive 6 weeks of NAC with OxFp (either full or modified dose) and surgery
4. Adequate full blood count: white blood cell (WBC)  $>3.0 \times 10^9/l$ ; platelets (PLTs)  $>100 \times 10^9/l$ .
5. Anaemia (Hb  $<10.0$  g/dl) is not an exclusion, but should be corrected by transfusion prior to
6. surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy can be given at the decision of the surgical and oncology teams.
7. Adequate renal biochemistry: glomerular filtration rate (GFR)  $>50$  ml/min as assessed by local standards
8. Adequate hepatobiliary function: bilirubin  $<1.5$  upper limit of normal (ULN) (patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study)
9. If female and of childbearing potential must agree to avoid pregnancy during and for 6 months after last dose of study treatment
10. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
11. Signed the Informed Consent Document for randomisation

FOxTROT 3 Inclusion Criteria

1. Patients need to be fit and suitable for mFOLFOXIRI. There is no fixed age cut-off, but most patients will be under 70 years.
2. pMMR/MSS tumour status for right sided tumours
3. Adequate full blood count: WBC  $>3.0 \times 10^9/l$ ; Neutrophils  $\geq 1.5 \times 10^9/l$ ; Plts  $>100 \times 10^9/l$ . Anaemia (Hb  $<100$  g/l) is not an exclusion, but should be corrected by transfusion prior to surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy

can be given at the decision of the surgical and oncology teams.

4. Adequate renal biochemistry: glomerular filtration rate (GFR) >50 ml/min as assessed by local standards
5. Adequate hepatobiliary function: bilirubin <1.5 upper limit of normal (ULN) (patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study)
6. If female and of childbearing potential must agree to avoid pregnancy during and for 6 months after last dose of study treatment
7. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
8. Signed the Informed Consent Document for randomisation

FOxTROT 4 inclusion criteria

1. pMMR/MSS colon adenocarcinoma (histologically confirmed).
2. Suitable for surgical resection and peri-operative SACT
3. No metastatic disease on routine staging investigations.
4. No prior treatment for bowel cancer
5. BRAFV600E mutation present in tumour biopsy (tested locally or centrally)
6. Adequate full blood count: WBC  $>3.0 \times 10^9/l$ ; Neutrophils  $\geq 1.5 \times 10^9/l$ ; Plts  $\geq 100 \times 10^9/l$ . Anaemia (Hb < 100 g/l) is not an exclusion but should be corrected by transfusion prior to surgery and SACT. If Hb remains low despite transfusions, surgery and SACT can be given at the decision of the surgical and oncology teams.
7. Adequate renal biochemistry: GFR >50 ml/min as assessed by local standards
8. Adequate hepatobiliary function: bilirubin < 1.5 x ULN (Patients with Gilbert's syndrome who have raised bilirubin, but otherwise normal liver function tests are eligible for the study.) AST /ALT <2.5 x ULN.
9. If female and of childbearing potential, must agree to avoid pregnancy during and for 6 months after the last dose of study treatment\*
10. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 6 months after the last dose of study treatment\*
11. Signed the Informed Consent Document for randomisation

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Previous inclusion criteria:

FOxTROT registration inclusion criteria:

1. Biopsy-confirmed adenocarcinoma of the colon (or upper rectum if too high for radiotherapy); high-grade dysplasia is acceptable with unequivocal radiological evidence of invasive cancer\*
2. Radiological stage T3-4, N0-2, M0
3. Patient being treated with curative intent
4. Tumour tissue is available for mismatch repair (MMR)/microsatellite instability (MSI) testing (local or central)
5. No clinical or radiological evidence of bowel obstruction
6. Age  $\geq 18$  years at the time of registration
7. Patient able and willing to provide written informed consent for the study

\* Patients with synchronous tumours are eligible if the most advanced tumour meets the criteria above (please note MMR/MSI testing requirements for randomisation depending upon the location of the most advanced tumour)

FOxTROT 2 inclusion criteria:

8. Patients will be unsuitable for mFOLFOXIRI due to oncologist assessed frailty or comorbidity
9. Proficient mismatch repair (pMMR)/MSS tumour status (for rt sided tumours)
10. Colorectal cancer (CRC) specialist-assessed fit to receive 6 weeks of NAC with OxFp (either full or modified dose) and surgery
11. Adequate full blood count: white blood cell (WBC)  $>3.0 \times 10^9/l$ ; platelets (PLTs)  $>100 \times 10^9/l$ . Anaemia (Hb  $<10.0$  g/dl) is not an exclusion, but should be corrected by transfusion prior to surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy can be given at the decision of the surgical and oncology teams.
12. Adequate renal biochemistry: glomerular filtration rate (GFR)  $>50$  ml/min as assessed by local standards
13. Adequate hepatobiliary function: bilirubin  $<1.5$  upper limit of normal (ULN) (patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study)
14. If female and of childbearing potential must agree to avoid pregnancy during and for 6 months after study treatment
15. If male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
16. Signed the Informed Consent Document for randomisation

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

Current exclusion criteria as of 14/08/2024:

FOxTROT registration exclusion criteria:

1. Any patient for whom radiotherapy is advised by the multidisciplinary team (MDT)
  2. Cases with a high index of suspicion of distant metastases or peritoneal nodules (cM1). However, cases with indeterminate abnormalities should be managed and investigated as per standard local MDT procedures and can be considered for trial entry if the MDT opinion is that these are considered most likely to be benign.
  3. Colonic obstruction that has not been defunctioned\*
  4. Women who are pregnant or breastfeeding
- \* Obstructed patients cannot be included in the FOxTROT trials, unless the obstruction has been

relieved. This would usually be by defunctioning. Patients may also be stented, but there is more limited safety data on this and these cases should be individually discussed with the Trial Management Group (TMG).

#### FOxTROT 2, FOxTROT 3 and FOxTROT 4 Exclusion Criteria:

1. Serious medical comorbidity, as assessed by the leading clinician (such as uncontrolled angina)
2. Any other malignant disease within the preceding 5 years with the exception of non-melanomatous skin cancer, carcinoma in situ and early-stage disease with a recurrence risk <10%
3. Known deficient mismatch repair (dMMR)/microsatellite Instability High (MSI-H) tumour status

#### FOxTROT 3 Additional Exclusion Criteria:

1. Known hypersensitivity to oxaliplatin, irinotecan or fluoropyrimidine therapy
2. Have a peripheral sensitive neuropathy with functional impairment
3. Have a severe chronic inflammatory bowel condition.
4. Known complete DPYD deficiency (homozygosity)
5. Recent or concomitant treatment with brivudine, sorivudine (or their chemically related analogues), St John's Wort.

#### FOxTROT 4 Additional Exclusion Criteria:

1. Impending bowel obstruction
2. Known hypersensitivity to oxaliplatin, or fluoropyrimidine therapy
3. Prior treatment with any RAF or EGFR inhibitors
4. Have a peripheral sensitive neuropathy with functional impairment
5. Have a severe chronic inflammatory bowel condition.
6. Known complete DPYD deficiency (homozygosity)
7. Recent or concomitant treatment with brivudine, sorivudine (or their chemically related analogues), St John's Wort.

#### FOxTROT 5 Exclusion Criteria:

1. Known pMMR or MSS/MSI-L colonic tumour status
2. Has a known additional malignancy that progressed or required active treatment within the past 2 years. Exceptions include adequately treated superficial skin cancers, superficial bladder cancers, and other in situ cancers
3. Is immunocompromised in the opinion of the investigator, is receiving any immunosuppressive medication, or has received systemic corticosteroids (>10mg prednisolone daily, or equivalent) within 7 days of first dose of study intervention. Use of inhaled steroids, local injection of steroids, topical steroids, and steroidal eye drops are allowed
4. Has an active autoimmune disease that has required systemic treatment in the past 2 years (i. e. with use of disease-modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g. levothyroxine) is not considered a form of systemic treatment
5. Experienced any of the following with prior immunotherapy: any Grade 3 or higher immune-related adverse reaction (irAR), any grade immune-related severe neurologic events (e.g. myasthenic syndrome/myasthenia gravis, encephalitis, Guillain-Barré syndrome, or transverse myelitis), any grade exfoliative dermatitis (Steven-Johnson syndrome, toxic epidermal necrolysis, or DRESS syndrome), any grade myocarditis. Non-clinically significant laboratory abnormalities are not exclusionary
6. Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to enrolment
7. Has any history of interstitial lung disease or pneumonitis
8. Cirrhosis or unstable liver or biliary disease per investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminaemia, oesophageal/gastric varices, or persistent jaundice

9. Has a history or current evidence of any medical condition, therapy, or laboratory abnormality that might confound the study results, interfere with their participation for the full duration of the study intervention, or indicate it is not in the best interests of the participant to participate, in the opinion of the investigator
  10. Has a history of allogenic stem cell transplantation or organ transplantation
  11. Has a history of congenital long QT syndrome
  12. Has a history or evidence of cardiac abnormalities such as serious, uncontrolled cardiac arrhythmia or clinically significant ECG abnormalities within the 6 months prior to enrolment
  13. Is receiving any other anticancer or experimental therapy
  14. Received a live vaccine within 30 days of planned start of study therapy
  15. Has documented presence of hepatitis B surface antigen (HBsAg) at screening or within 3 months prior to enrolment
  16. Has a positive hepatitis C virus (HCV) antibody test result at screening or within 3 months prior to enrolment. Note: Participants with a positive HCV antibody test result due to prior resolved disease can be enrolled, only if a confirmatory HCV RNA test is obtained
  17. Has a positive HCV RNA test result at screening or within 3 months prior to enrolment. Note: The HCV RNA test is optional and participants with negative HCV antibody test are not required to undergo HCV RNA testing as well
  18. Is considered, in the investigator's opinion, a poor medical risk due to severe, uncontrolled medical disorder, non-malignant systemic disease, or active infection requiring systemic therapy.
  19. Has known history of human immunodeficiency virus (HIV) infection (unless the specific criteria in the FOxTROT 5 protocol are met)
  20. A known history of severe allergic and/or anaphylactic reactions to chimeric, human or humanized antibodies, fusion proteins, or to dostarlimab or its excipients
- 

Previous exclusion criteria as of 17/10/2023 to 14/08/2024:

FOxTROT registration exclusion criteria:

1. Any patient for whom radiotherapy is advised by the multidisciplinary team (MDT)
  2. Cases with a high index of suspicion of distant metastases or peritoneal nodules (cM1). However, cases with indeterminate abnormalities should be managed and investigated as per standard local MDT procedures and can be considered for trial entry if the MDT opinion is that these are considered most likely to be benign.
  3. Colonic obstruction that has not been defunctioned\*
  4. Women who are pregnant or breastfeeding
- \* Obstructed patients cannot be included in the FOxTROT trials, unless the obstruction has been relieved. This would usually be by defunctioning. Patients may also be stented, but there is more limited safety data on this and these cases should be individually discussed with the Trial Management Group (TMG).

FOxTROT 2, FOxTROT 3 and FOxTROT 4 Exclusion Criteria:

1. Serious medical comorbidity, as assessed by the leading clinician (such as uncontrolled angina)
2. Any other malignant disease within the preceding 5 years with the exception of non-melanomatous skin cancer, carcinoma in situ and early-stage disease with a recurrence risk <10%
3. Known deficient mismatch repair (dMMR)/microsatellite Instability High (MSI-H) tumour status

FOxTROT 3 Additional Exclusion Criteria:

1. Known hypersensitivity to oxaliplatin, irinotecan or fluoropyrimidine therapy
2. Have a peripheral sensitive neuropathy with functional impairment
3. Have a severe chronic inflammatory bowel condition.

4. Known complete DPYD deficiency (homozygosity)
5. Recent or concomitant treatment with brivudine, sorivudine (or their chemically related analogues), St John's Wort.

FOxTROT 4 Additional Exclusion Criteria:

1. Impending bowel obstruction
2. Known hypersensitivity to oxaliplatin, or fluoropyrimidine therapy
3. Prior treatment with any RAF or EGFR inhibitors
4. Have a peripheral sensitive neuropathy with functional impairment
5. Have a severe chronic inflammatory bowel condition.
6. Known complete DPYD deficiency (homozygosity)
7. Recent or concomitant treatment with brivudine, sorivudine (or their chemically related analogues), St John's Wort.

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Previous exclusion criteria:

FOxTROT randomisation exclusion criteria:

1. Any patient for whom radiotherapy is advised by the multidisciplinary team (MDT)
  2. Strong evidence of distant metastases or peritoneal nodules (cM1), however patients with lung lesions of uncertain significance (<5 mm) are eligible
  3. Peritonitis (secondary to perforated tumour)
  4. Colonic obstruction that has not been defunctioned\*
- \* Obstructed patients cannot be included in the FOxTROT trials, unless the obstruction has been relieved. This would usually be by defunctioning. Patients may also be stented, but there is more limited safety data on this and these cases should be individually discussed with the Trial Management Group (TMG).

FOxTROT 2 exclusion criteria:

5. Serious medical comorbidity, as assessed by the leading clinician (such as uncontrolled angina)
6. Any other malignant disease within the preceding 5 years with the exception of non-melanomatous skin cancer, carcinoma in situ and early-stage disease with a recurrence risk <10%
7. Known deficient mismatch repair (dMMR)/microsatellite Instability High (MSI-H) tumour status

**Date of first enrolment**

07/02/2022

**Date of final enrolment**

01/04/2027

## Locations

**Countries of recruitment**

United Kingdom

England

Scotland

Wales

Australia

France

India

Netherlands

Sweden

**Study participating centre**

**Airedale General Hospital**

Skipton Rd

Steeton

Keighley

United Kingdom

BD20 6TD

**Study participating centre**

**St Bartholomew's Hospital**

W Smithfield

London

United Kingdom

EC1A 7BE

**Study participating centre**

**Ysbyty Gwynedd**

Penrhosgarnedd

Bangor

United Kingdom

LL57 2PW

**Study participating centre**

**Bradford Royal Infirmary**

Duckworth Ln

Bradford

United Kingdom

BD9 6RJ

**Study participating centre**

**Calderdale Rotal Hospital and Huddersfield Royal Infirmary**

Acre St  
Lindley  
Huddersfield  
United Kingdom  
HD3 3EA

**Study participating centre**

**Addenbrooke's Hospital**

Hills Rd  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**West Middlesex University Hospital**

Twickenham Rd  
Isleworth  
United Kingdom  
TW7 6AF

**Study participating centre**

**Chesterfield Royal Hospital**

Chesterfield Rd  
Calow  
Chesterfield  
United Kingdom  
S44 5BL

**Study participating centre**

**Countess of Chester Hospital**

Liverpool Rd  
Chester  
United Kingdom  
CH2 1UL

**Study participating centre**

**Darlington Memorial Hospital**

Hollyhurst Rd

Darlington  
United Kingdom  
DL3 6HX

**Study participating centre**  
**Macclesfield District General Hospital**  
Victoria Rd  
Macclesfield  
United Kingdom  
SK10 3BL

**Study participating centre**  
**Ipswich Hospital**  
Heath Rd  
Ipswich  
United Kingdom  
IP4 5PD

**Study participating centre**  
**Conquest Hospital**  
The Ridge  
Saint Leonards-on-Sea  
United Kingdom  
TN37 7RD

**Study participating centre**  
**Bensham Hospital**  
Fontwell Dr  
Gateshead  
United Kingdom  
NE8 4YL

**Study participating centre**  
**Great Western Hospital**  
Marlborough Rd  
Swindon  
United Kingdom  
SN3 6BB

**Study participating centre**  
**Basingstoke and North Hampshire Hospital**  
Aldermaston Rd  
Basingstoke  
United Kingdom  
RG24 9NA

**Study participating centre**  
**Charing Cross Hospital and St Mary's**  
Fulham Palace Rd  
London  
United Kingdom  
W6 8RF

**Study participating centre**  
**Kettering General Hospital**  
Rothwell Rd  
Kettering  
United Kingdom  
NN16 8UZ

**Study participating centre**  
**St James's University Hospital**  
Beckett St  
Harehills  
Leeds  
United Kingdom  
LS9 7TF

**Study participating centre**  
**Queen Elizabeth Hospital & Lewisham Hospital**  
Stadium Rd  
London  
United Kingdom  
SE18 4QH

**Study participating centre**  
**Royal Liverpool University Hospital**  
Prescot St

Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**  
**Manchester Royal Infirmary**  
Oxford Rd  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**  
**Crosshouse Hospital**  
Kilmarnock Rd  
Crosshouse  
Kilmarnock  
United Kingdom  
KA2 0BE

**Study participating centre**  
**Queen Margaret Hospital and Victoria Hospital**  
Whitefield Rd  
Dunfermline  
United Kingdom  
KY12 0SU

**Study participating centre**  
**Forth Valley Royal Hospital**  
Stirling Rd  
Larbert  
United Kingdom  
FK5 4WR

**Study participating centre**  
**Beatson West of Scotland Cancer Centre**  
1053 Great Western Rd  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**Royal Edinburgh Hospital**  
Morningside Pl  
Edinburgh  
United Kingdom  
EH10 5HF

**Study participating centre**  
**Norfolk & Norwich University Hospital**  
Colney Ln  
Colney  
Norwich  
United Kingdom  
NR4 7UY

**Study participating centre**  
**Northampton General Hospital**  
Cliftonville  
Northampton  
United Kingdom  
NN1 5BD

**Study participating centre**  
**Hexham General Hospital**  
Corbridge Rd  
Hexham  
United Kingdom  
NE46 1QJ

**Study participating centre**  
**Queen Alexandra Hospital**  
Cosham  
Portsmouth  
United Kingdom  
PO6 3LY

**Study participating centre**  
**Royal Cornwall Hospital**  
Treliske  
Truro

United Kingdom  
TR1 3LJ

**Study participating centre**  
**Royal Devon and Exeter Hospital**  
Barrack Rd  
Exeter  
United Kingdom  
EX2 5DW

**Study participating centre**  
**Royal Free Hospital**  
Pond St  
London  
United Kingdom  
NW3 2QG

**Study participating centre**  
**Royal United Hospital**  
Combe Park  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**  
**Weston Park Cancer Centre**  
Whitham Rd  
Broomhall  
Sheffield  
United Kingdom  
S10 2SJ

**Study participating centre**  
**St George's Hospital**  
Blackshaw Rd  
London  
United Kingdom  
SW17 0QT

**Study participating centre**  
**Musgrove Park Hospital**  
Parkfield Dr  
Taunton  
United Kingdom  
TA1 5DA

**Study participating centre**  
**The Christie**  
Wilmslow Rd  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**  
**Clatterbridge Cancer Centre Liverpool and Clatterbridge Cancer Centre Wirral**  
Clatterbridge Rd,  
Birkenhead  
Wirral  
United Kingdom  
CH63 4JY

**Study participating centre**  
**The Royal Marsden Hospital (Chelsea and Sutton)**  
203 Fulham Rd  
London  
United Kingdom  
SW3 6JJ

**Study participating centre**  
**Royal Surrey County Hospital**  
Egerton Rd  
Guildford  
United Kingdom  
GU2 7XX

**Study participating centre**  
**Harrogate District Hospital**  
Lancaster Park Rd

Harrogate  
United Kingdom  
HG2 7SX

**Study participating centre**  
**Lincoln County Hospital**  
Greetwell Rd  
Lincoln  
United Kingdom  
LN2 5QY

**Study participating centre**  
**UCL Cancer Institute**  
72 Huntley St  
London  
United Kingdom  
WC1E 6DD

**Study participating centre**  
**Bristol Cancer Centre**  
22 Horfield Rd  
Bristol  
United Kingdom  
BS2 8ED

**Study participating centre**  
**University Hospital Coventry**  
Clifford Bridge Rd  
Coventry  
United Kingdom  
CV2 2DX

**Study participating centre**  
**Poole Hospital and Royal Bournemouth Hospital**  
Longfleet Rd  
Poole  
United Kingdom  
BH15 2JB

**Study participating centre**

**Royal Derby Hospital**

Uttoxeter Rd  
Derby  
United Kingdom  
DE22 3NE

**Study participating centre**

**Royal Stoke University Hospital**

Newcastle Rd  
Stoke-on-Trent  
United Kingdom  
ST4 6QG

**Study participating centre**

**Derriford Hospital**

Derriford Rd  
Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre**

**Leicester General Hospital**

Gwendolen Rd  
Leicester  
United Kingdom  
LE5 4PW

**Study participating centre**

**Velindre Cancer Centre**

Velindre Rd  
Cardiff  
United Kingdom  
CF14 2TL

**Study participating centre**

**Walsall Manor Hospital**

Moat Rd  
Walsall  
United Kingdom  
WS2 9PS

**Study participating centre**  
**Worcestershire Royal Hospital**  
Charles Hastings Way  
Worcester  
United Kingdom  
WR5 1DD

**Study participating centre**  
**Royal Albert Edward Infirmary**  
Wigan Ln  
Wigan  
United Kingdom  
WN1 2NN

**Study participating centre**  
**York Teaching Hospital**  
Wigginton Rd  
Clifton  
York  
United Kingdom  
YO31 8HE

**Study participating centre**  
**Dorset County Hospital**  
Williams Ave  
Dorchester  
United Kingdom  
DT1 2JY

**Study participating centre**  
**Colchester Hospital**  
Turner Rd  
Colchester  
United Kingdom  
CO4 5JL

**Study participating centre**

**George Eliot Hospital**

College St  
Nuneaton  
United Kingdom  
CV10 7DJ

**Study participating centre**

**University Hospital Monklands**

Monkscourt Ave  
Airdrie  
United Kingdom  
ML6 0JS

**Study participating centre**

**University Hospital of North Tees**

Hardwick Rd  
Hardwick  
Stockton-on-Tees  
United Kingdom  
TS19 8PE

**Study participating centre**

**The James Cook University Hospital**

Middlesbrough  
United Kingdom  
TS4 3BS

**Study participating centre**

**Warwick Hospital**

Lakin Rd  
Warwick  
United Kingdom  
CV34 5BW

**Study participating centre**

**East Yorkshire Hospitals NHS Trust (head Office)**

Castle Hill Hospital  
Castle Road  
Cottingham  
United Kingdom  
HU16 5JQ

**Study participating centre**  
**Mid Cheshire Hospitals NHS Foundation Trust**  
Leighton Hospital  
Leighton  
Crewe  
United Kingdom  
CW1 4QJ

**Study participating centre**  
**Milton Keynes University Hospital**  
Standing Way  
Eaglestone  
Milton Keynes  
United Kingdom  
MK6 5LD

**Study participating centre**  
**University Hospital Crosshouse**  
Kilmarnock Road  
Kilmarnock  
United Kingdom  
KA2 0BE

**Study participating centre**  
**Queen Margaret Hospital**  
Whitefield Road  
Dunfermline  
United Kingdom  
KY12 0SU

**Study participating centre**  
**Victoria Hospital**  
Hayfield Road  
Kirkcaldy  
United Kingdom  
KY2 5AH

**Study participating centre**

**Ninewells Hospital**  
Ninewells Avenue  
Dundee  
United Kingdom  
DD1 9SY

**Study participating centre**  
**Churchill Hospital**  
Churchill Hospital  
Old Road  
Headington  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**  
**Singleton Hospital**  
Sketty Lane  
Sketty  
Swansea  
United Kingdom  
SA2 8QA

**Study participating centre**  
**Queen Elizabeth Hospital**  
Mindelsohn Way  
Edgbaston  
Birmingham  
United Kingdom  
B15 2GW

**Study participating centre**  
**Yeovil Hospital Bcsc**  
Yeovil District Hospital  
Higher Kingston  
Yeovil  
United Kingdom  
BA21 4AT

**Study participating centre**

**Christian Medical College and Hospital (Local Sponsor for FOxTROT 2 only)**

Brown Rd, CMC Campus

Ludhiana

India

141008

**Study participating centre**

**CHU DIJON (Local Sponsor for FOxTROT 2 only)**

1 Rue du Professeur Marion

Dijon

France

21000

## Sponsor information

**Organisation**

University of Leeds

**ROR**

<https://ror.org/024mrx33>

## Funder(s)

**Funder type**

Charity

**Funder Name**

Yorkshire Cancer Research

**Alternative Name(s)**

YCR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

**Funder Name**

Merck

**Funder Name**

Pierre Fabre

**Funder Name**

GSK

## Results and Publications

**Individual participant data (IPD) sharing plan**

De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact [CTRU-DataAccess@leeds.ac.uk](mailto:CTRU-DataAccess@leeds.ac.uk) in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

**IPD sharing plan summary**

Stored in non-publicly available repository, Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes

