FOxTROT Newsletter

Bringing you all the key news about the FOXTROT Platform, in one place.

Welcome to our latest newsletter for the FOxTROT Platform!

Prof. Jenny Seligmann, Chief Investigator, University of Leeds

We use these newsletters to give site teams an update on trial progress and provide useful tips and reminders. We will share news about the platform and also other relevant developments in the field.

Prof. Dion Morton, Co-Chief Investigator, University of Birmingham

We want the newsletters to be useful and interesting for you so please get in touch via foxtrot@leeds.ac.uk with any suggestions or comments for future editions.

Website – New Content and "Researchers" Section Launch

➢ We have made some changes to the FOxTROT website recently and are continuing to improve the content. We will be adding new videos and information over the coming months. Please direct potential participants to our website for an overview of the platform.

https://ctru.leeds.ac.uk/foxtrot/

➢ The website now also has a dedicated section for Researchers: https://ctru.leeds.ac.uk/foxtrot/for-researchers/.

There you will be able to access the most current trial documentation, including Protocols, Patient Information Sheets and QoL booklets.

The access will be by username and password protected. The FOxTROT team will be contacting you soon to give you these details.

As always, we are keen for feedback from our sites. Additionally, if you are looking for something that cannot be found on the website, please contact us at foxtrot@leeds.ac.uk.

FOxTROT

FOXTROT Sites - Updates

A full list of the hospitals participating in FOxTROT can be found here:
https://ctru.leeds.ac.uk/foxtrot/for-patients/is-my-hospital-recruiting/

**FOxTROT 2
58 Hospitals**

**FOxTROT 4
18 Hospitals**

**FOxTROT 3
51 Hospitals**

**FOxTROT 5
3 Hospitals**

A special thank you to:

- ✓ **Glan Clwyd, Derriford and Salisbury District Hospital** for recently opening for FOxTROT 2 and 3

- ✓ **Colchester General Hospita**l for recently opening for FOxTROT 4

- ✓ **Churchill Hospital** for recently opening for FOxTROT 5

Planned Protocol Updates

➢ **FOxTROT 2 and 3**

We are working on various updates and corrections to the FOxTROT 2 and FOxTROT 3 protocols and patient information sheets. We will notify all sites when this substantial amendment has been approved.

➢ **FOxTROT 4 redesign**

Due to some recruitment challenges with FOxTROT 4, the study design is being adapted to move from a randomised trial to a single arm trial so all participants will receive the investigational encorafenib and cetuximab treatment. The FOxTROT 4 team will keep you updated on this substantial amendment, so watch this space for further developments!

Planned Protocol Updates

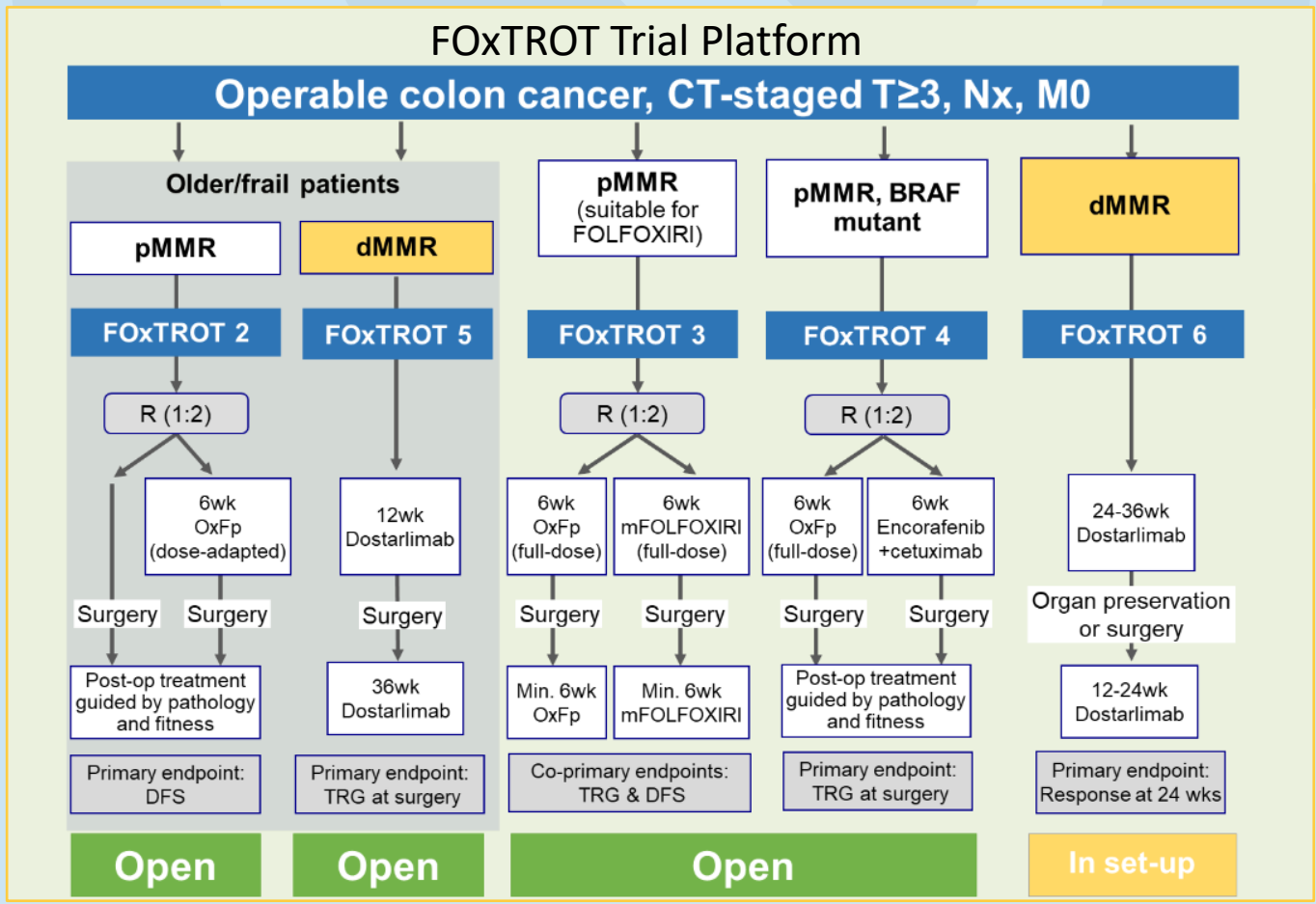**FOxTROT 5 has opened – New dMMR trial arm for FOxTROT Trial Platform**

FOxTROT 5 opened to recruitment in November 2024!

We are setting this protocol up at 20 sites. FOxTROT 5 has been added to the Platform as part of Substantial Amendment SA07 – we are contacting sites individually with details of how to implement this amendment, depending on whether they are participating in FOxTROT 5 or not.

Trial details

Population	older and/or frail patients with untreated locally advanced dMMR/MSI-H colorectal cancer
Treatment	12 weeks of neoadjuvant dostarlimab (an anti-PD1 monoclonal antibody) prior to surgery with curative intent, followed by 36 weeks of post-operative dostarlimab
Aim	to investigate if this treatment will demonstrate similar efficacy to that seen in younger and fitter populations.

With **FOxTROT 2** and **FOxTROT 5**, the FOxTROT trial platform will be in a unique position to offer the under-served older and/or frail population two clinical trial arms depending on their MMR/MSI status.

FOxTROT Trial Platform

Operable colon cancer, CT-staged T≥3, Nx, M0

Older/frail patients

pMMR	dMMR	pMMR (suitable for FOLFOXIRI)	pMMR, BRAF mutant	dMMR
FOxTROT 2	FOxTROT 5	FOxTROT 3	FOxTROT 4	FOxTROT 6
R (1:2)		R (1:2)	R (1:2)	
6wk OxFp (dose-adapted)	12wk Dostarlimab	6wk OxFp (full-dose) / 6wk mFOLFOXIRI (full-dose)	6wk OxFp (full-dose) / 6wk Encorafenib +cetuximab	24-36wk Dostarlimab
Surgery / Surgery	Surgery	Surgery / Surgery	Surgery / Surgery	Organ preservation or surgery
Post-op treatment guided by pathology and fitness	36wk Dostarlimab	Min. 6wk OxFp / Min. 6wk mFOLFOXIRI	Post-op treatment guided by pathology and fitness	12-24wk Dostarlimab
Primary endpoint: DFS	Primary endpoint: TRG at surgery	Co-primary endpoints: TRG & DFS	Primary endpoint: TRG at surgery	Primary endpoint: Response at 24 wks
Open	Open	Open		In set-up

This Month's Recruitment Figures

So far in **January** we have randomised/enrolled 28 participants, which is fantastic!

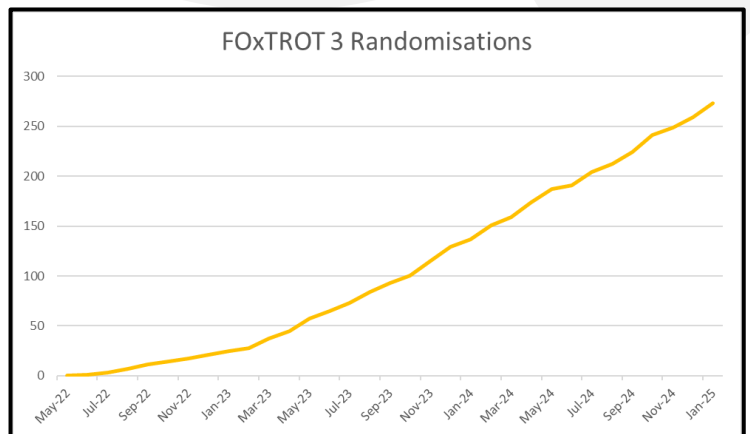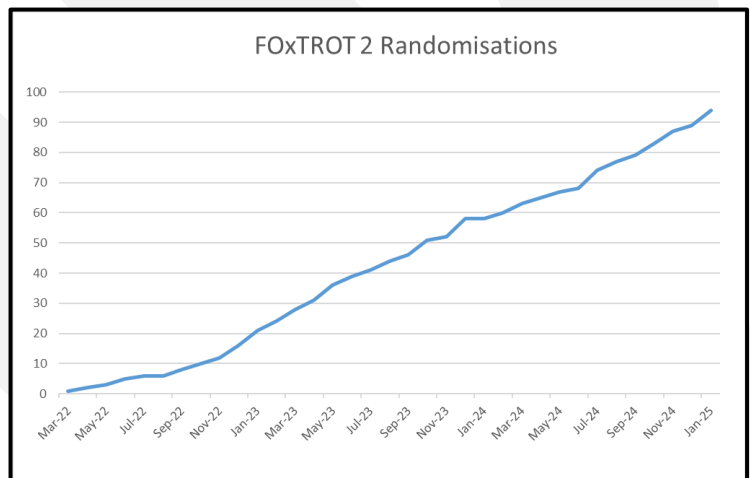| FOxTROT 2	FOxTROT 3	FOxTROT 4	FOxTROT 5
8 (1 France, 2 India)	15	3	2

Over 14th and 15th of Jan we managed to randomise/enroll a patient on each trial arm! Please do keep up the hard work and thank you to all the sites that have contributed to this month's recruitment!

Recruitment

It has been a good few months for FOXTROT recruitment.

Total Recruitment: 368

Trial Arm	Recruitment
FOxTROT 2	130 participants randomised (13 France, 23 India)
FOxTROT 3	274 participants randomised
FOxTROT 4	10 participants randomised
FOxTROT 5	2 participants enrolled

FOxTROT 2 Randomisations

FOxTROT 3 Randomisations

Helpful Tips and Advice to Help with Recruitment

FOxTROT 4 Sites

In order to identify suitable FOxTROT 4 patients as quickly as possible, biomarker testing (RAS, BRAF, MSI/MMR) should be requested at first MDT discussion.

➢ Good communication with your local Pathologist is key!
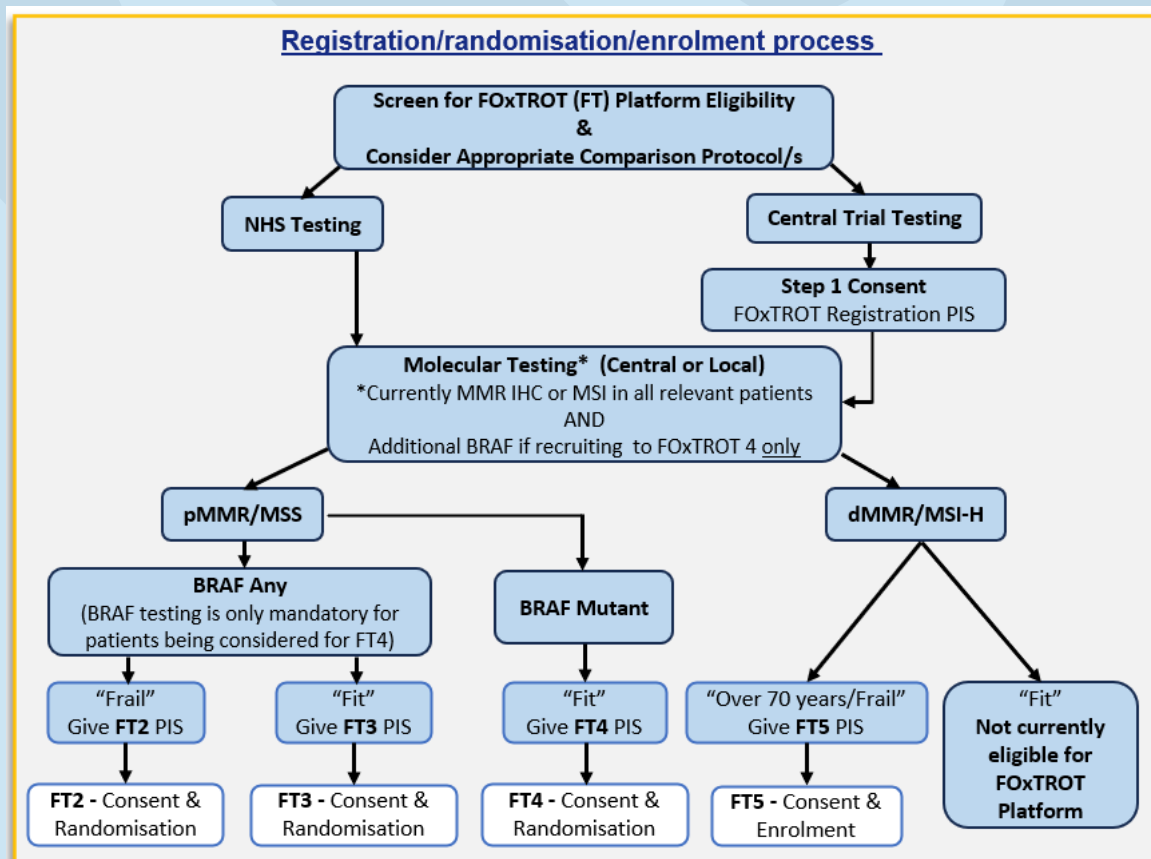➢ Chase Pathology until results are back.

BRAF testing is also available through Central Panel Testing (detailed in the Molecular Testing Guidance document).

For BRAF wild type patients, consider if they would be suitable for FOxTROT 2 or FOxTROT 3 (pMMR) or FOxTROT 5 (dMMR).

IMPORTANT: Consider referring patients to other local FOxTROT sites if your site does not offer the other FOxTROT trial arms.

Molecular Testing Guidance

Information on molecular testing pathways can be found on the FOxTROT website once you have logged into the 'Researchers' section. It contains useful information on ideal molecular testing pathways that should be adopted at sites and how to use central testing. for the FOxTROT trial arms – link is here.

Helpful Tips and Advice to Help with Recruitment

All Sites (FOxTROT 2, FOXTROT 3 and FOxTROT 5) – Referrals

Please consider referring any pMMR BRAF^{V600E} mutant patients to a local FOxTROT 4 site (see table below for open FOxTROT 4 sites)

Patients can have surgery and adjuvant chemotherapy at the referring site, so just travelling to the FOxTROT 4 site for the 3 cycles of encorafenib and cetuximab.

Central BRAF testing is available through Central Panel Testing (details on how to access this are on the 'Molecular Testing Guidance' document and results are available approximately 7 days after receipt of the block.

There is a short PIS that explains this testing and same day consent (and remote consent) is acceptable.

FOxTROT 4 Open Sites	
East Suffolk & North Essex NHSFT - Ipswich Hospital	East Suffolk & North Essex NHSFT - Colchester General Hospital
Leeds Teaching Hospitals NHS Trust - St James's Hospital	United Lincolnshire NHS Trust - Lincoln County Hospital & Pilgrim Hospital Boston
NHS Greater Glasgow and Clyde - Beatson West of Scotland Cancer Centre	Queen's Hospital Burton - University Hospitals of Derby and Burton NHSFT
Velindre University NHS Trust - Velindre Cancer Centre, Cardiff	Milton Keynes University Hospital NHSFT
University College London - NHSFT	Sheffield Teaching Hospitals NHSFT - Weston Park Hospital
Hull University Teaching Hospitals NHSFT - Castle Hill Hospital	NHS Tayside
Royal Devon University Healthcare NHSFT - Royal Devon and Exeter Hospital	Royal Cornwall Hospitals NHS Trust
NHS Fife - Victoria Hospital Kirkcaldy	Somerset NHSFT - Musgrove Park
Royal Free London NHS Foundation Trust - Royal Free London Hospital and Chase Farm Hospital	University Hospitals Birmingham NHSFT - Queen Elizabeth Hospital

If you would like to discuss the molecular testing pathways for your trial arm(s) and/or help with referrals, please contact us at FOxTROT@leeds.ac.uk.

Important Reminders

Authorised Personnel Log (APL) Return (whole document)

When sending an updated APL (same as a delegation log) to the CTRU please send a scan of the entire APL rather than just 1 page.

This enables any staff who have left to be removed from databases/contacts lists and to have the correct duties identified as different versions of APLs have different numbers for delegated roles. This will help us to maintain our records accurate.

TRG Completion

Please ensure that the Tumour Regression Grade (TRG) field is completed on the Pathology eCRF – this is important for our analysis. It is the site's pathologist responsibility to provide this.

QoL Return

The original QoL (paper document) must be posted to the CTRU. Please use pre-labelled envelopes to post QoLs back to CTRU.

QoL forms should not be scanned, printed or copied nor retained at site. These should not be sent electronically.

Central Gene Panel Testing

The 50 Gene Panel Testing should only be requested at the Baseline setting and not once the participant has started trial treatment.

Ordering encorafenib

For FOxTROT 4 sites - Please only place an encorafenib order once you have randomised a patient to the EC arm.

Ordering ctDNA Kits

To order more kits for the ctDNA samples please contact the Birmingham lab team directly at foxtrot@lists.bham.ac.uk. The CTRU will not be able to order these for you.

ctDNA Testing Explained

Baseline ctDNA samples should be taken for all consented participants prior to randomisation. If the ctDNA sample has not been taken prior to randomisation, it is acceptable to take it post-randomisation but before start of trial treatment.

We aim to minimise venepuncture where possible. It is therefore hoped the ctDNA sample can be taken at the time of pre-randomisation screening bloods.

Also, **optional ctDNA testing** now requires just two ctDNA tubes of blood as opposed to the 2-4 tubes detailed in the protocol. Please can sites adhere to this change in order to save sample kits which central labs are currently short on.

FOxTROT

Locked out of MACRO?

If you're locked out of MACRO and have not received a password reset email, have you tried this?

1. Please close all windows down before trying again.

2. Always use Microsoft Edge to access MACRO.

3. If you do receive a password reset email, always type your password, do not copy & paste it.

4. If this fails, get in touch with us!

Contact Us

General enquiries: foxtrot@leeds.ac.uk

24 Hour Randomisation: https://lictr.leeds.ac.uk/webrand/

MACRO database: https://ctru.leeds.ac.uk/trial-systems/macro/

Safety reporting: Enter data on MACRO and send queries to

foxtrot@leeds.ac.uk

Website: https://ctru.leeds.ac.uk/foxtrot/

Thank you!