

FOX TROT Platform News Bulletin

It has been a busy few months in the FOX TROT platform, so we wanted to highlight some of the key changes recently implemented across the platform

Urgent Safety Measure

Recently the FOX TROT trial implemented an urgent safety measure. As part of this we contacted all hospitals to outline the FOX TROT platform DPYD guidelines, changes to the FOX TROT eligibility and to request additional information on the DPYD status of participants already randomised.

Here is a quick break down of the urgent safety measures that your site must now be working to:

Protocol changes

- Additional exclusion criteria in FOX TROT 2, FOX TROT 3 and FOX TROT 4:
 - Known DPYD heterozygous germline variants with recommended dose reduction of fluoropyrimidine-based therapy greater than 50% or avoidance of fluoropyrimidine-based therapies
- Mandatory DPYD assessment at baseline
- Additional general guidance around the dose modifications for participants with a DPYD germline mutation

Actions from sites

- Acknowledgement from all sites of the serious breach
- Work to the new guidance outlined above
- When randomising a participant to FT2, FT3 or FT4 please add a comment to the Randomisation eligibility form (F02) to note this patient has been recruited under the USM guidance
- Providing a file note of DPYD testing for all randomised patient signed by the PI

The amended protocols have been submitted for regulatory approval and will be shared as soon as this is in place.

Treatment Regimes and Dose Modification

Guidance on the trial treatment regimens and any dose modifications can be found in the platform protocols. Please refer to the relevant study arm protocol table below which shows where to find guidance on:

- Treatment regimes
- Supportive medication
- Dose modifications (e.g. dose reductions if relevant, delays or discontinuations)
- Management of toxicities

If any treatment is modified, please make sure the relevant treatment forms (F06/F07/F12) are completed accordingly on the MACRO database.

Trial arm	Treatment Regimens	Supportive medication	Dose Modifications	Management of Toxicities
FT2	Appendix C			
FT3	Appendix B (mFOLFOXIRI) Appendix C (OxMdG/OxCap)			
FT4	Appendix B (EC) Appendix C (OxFp)			
FT5	Section 13.1	Section 13.7	Section 13.6	Section 13.6

Thank you!

We really appreciate all your support and co-operation with implementing this amendment

