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FOXFIRE: an open-label randomised phase III trial of 5-Fluorouracil, OXaliplatin and Folinic acid +/- Interventional Radio-Embolisation as first line treatment for patients with unresectable liver-only or liver-predominant metastatic colorectal cancer

Submission date 20/06/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 29/08/2008	**Overall study status** Completed	
Last Edited 26/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-chemotherapy-with-without-radioembolisation-for-bowel-cancer-that-has-spread-to-the-liver-foxfire

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
OCTO_009

Study information

Scientific Title
FOXFIRE: an open-label randomised phase III trial of 5-Fluorouracil, OXaliplatin and Folinic acid +/- Interventional Radio-Embolisation as first line treatment for patients with unresectable liver-only or liver-predominant metastatic colorectal cancer

Acronym
FOXFIRE

Study objectives
Combination of chemotherapy and radioembolisation will improve the outcome for patients with colorectal cancer plus liver only/ dominant metastases compared with chemotherapy alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Berkshire Regional Ethics Committee (REC), 16/03/2009, ref: 09/H0505/1

Study design
Open-label multicentre randomised controlled phase III study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colorectal cancer with liver only or liver dominant metastases

Interventions
Arm A: Systemic OxMdG chemotherapy: oxaliplatin, folinic acid (FA) and 5-fluorouracil (5-FU)
Arm B: SIR-Spheres® radioembolisation (RE) plus systemic OxMdG chemotherapy: oxaliplatin, FA and 5-FU

Therapy schedule: 14 days per cycle, 12 cycles maximum. Radioembolisation occurs on Day 3 of the 2nd cycle.

The total duration of follow-up is 24 months. After this period, only mortality will be recorded.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
5-fluorouracil, oxaliplatin, folinic acid

Primary outcome(s)
Overall survival (OS)

Key secondary outcome(s))
1. Progression free survival (PFS)
2. Liver-specific PFS
3. Safety and toxicity
4. Healthcare costs/health economics
5. Quality of life, assessed with the euroqol EQ-5D questionnaire at baseline, start of cycle 4 and cycle 12, month 24 and 36, and at progression
6. Response rate
7. Resection rate
8. Percentage of patients receiving second line treatment
9. Interval from randomisation to start of second line treatment

Completion date
31/10/2016

Eligibility

Key inclusion criteria
1. Histologically confirmed colorectal cancer with liver-only or liver-dominant (see also 'limited and/or resectable extra-hepatic disease' criterion below) metastases not amenable to curative (R0) liver surgical resection (see also exclusion criteria below), which must be agreed at local multi-disciplinary team (MDT) meeting with hepatic surgery & radiology representation.
2. Unequivocal and measurable CT evidence of liver metastases which are not treatable by surgical resection or local ablation with curative intent at the time of trial entry
3. Both males and females, age >18 years
4. WHO performance status of 0-1
5. Life expectancy >3 months
6. Eligible for systemic chemotherapy as first-line treatment for metastatic colorectal cancer
7. Adequate haematological, renal and hepatic function (recorded within 29 days of randomisation) as follows:
7.1. Serum creatinine <=1.5 x ULN
7.2. Serum bilirubin <=1 x ULN
7.3. Absolute neutrophil count >1.5 x 10^9/L
7.4. Platelets >100 x 10^9/L
7.5. Albumin >=30 g/L
8. Limited and/or resectable extra-hepatic disease (EHD) defined as**:
8.1. Lung lesions (<=5 metastases of <=1 cm each which are immediately amenable to surgery or ablation, without requiring initial chemotherapy for downstaging)
8.2. Positron emission tomography (PET) or biopsy negative lesions (optional if performed)
8.3. Abdominal or perihepatic lymph nodes less than 2 cm in longest diameter
8.4. Presence of detectable extra-hepatic tumour that can be resected. This includes asymptomatic synchronous primary colorectal tumours (i.e. with unresectable liver metastases)
** These criteria will generally be considered mutually exclusive and patients with more than one criterion must be discussed with the TMG

9. Suitable for all aspects of treatment determined by clinical assessment undertaken by the Investigator
10. Female patients must either be post-menopausal or, if pre-menopausal and sexually active, using an acceptable method of contraception
11. Male patients, if sexually active with a pre-menopausal partner, must be using an appropriate method of contraception
12. Willing and able to provide written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
549

Key exclusion criteria
1. Liver metastases amenable to curative resection at the time of study entry, unless the patient has limited EHD as defined above
2. Pregnancy or breastfeeding
3. Evidence of ascites, cirrhosis or portal hypertension (as determined by clinical or radiological assessment)
4. Tumour involvement of, or thrombosis leading to complete occlusion of, the main portal vein is an absolute contra-indication to trial entry. Previous liver resection(s) or previous portal vein embolisation are not exclusion criteria to entry into the clinical trial. Patients with complicated surgical histories involving embolisation and resection should be discussed with the TMG prior to study entry for clarification of safety and eligibility.
5. Previous radiotherapy to the upper abdomen or upper lumbar spine
6. Other active malignancy within the past 5 years, excluding colorectal cancer and non-melanoma skin cancers
7. Non-malignant disease that would render the patient ineligible for treatment at the discretion of the investigator
8. Equivocal, immeasurable, or unevaluable metastases in the liver
9. Patients with unequivocal evidence of bone metastasis are not permitted to enter the trial. Patients with a single equivocal lesion of uncertain significance should be discussed with the FOXFIRE Trial Office.
10. Dose limiting toxicity associated with previous 5-FU or oxaliplatin chemotherapy.
11. Previous chemotherapy for metastatic colorectal cancer. Adjuvant chemotherapy for colorectal cancer is not an exclusion criterion provided that the last dose of adjuvant chemotherapy was completed at least 6 months prior to entry into this study. Patients who have previously received oxaliplatin-based adjuvant chemotherapy regimens should be discussed with

the FOXFIRE Trial Office
12. Peripheral neuropathy on clinical examination >grade 1 (National Cancer Institute Common Toxicity Criteria [NCI-CTC v.3])

Date of first enrolment
13/11/2009

Date of final enrolment
31/10/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oncology Clinical Trials Office (OCTO)
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Bobby Moore Fund for Cancer Research UK

Funder Name

Sirtex (educational grant, providing SIR-Spheres® for the study free of charge)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the FOXFIRE trial team: Ricky Sharma (ricky.sharma@oncology.ox.ac.uk) and the trial management team (octo-foxfire@oncology.ox.ac.uk). All requests will be considered on an individual basis and in accordance with a data sharing agreement.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2017		Yes	No
Protocol article	protocol	09/07/2014		Yes	No
Basic results		13/09/2017	14/05/2018	No	No
Plain English results			26/10/2022	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes