Clinical Study in Colorectal Cancer

FOXFIRE Global

The FOXFIREGlobal Study

SIR-Spheres® microspheres + FOLFOX *versus* FOLFOX Alone (with or without bevacizumab) in Patients with Unresectable Liver Metastases from Colorectal Cancer

Randomized controlled study evaluating SIR-Spheres microspheres in combination with FOLFOX chemotherapy *vs.* FOLFOX chemotherapy alone for the first-line treatment of unresectable liver-only or liver-predominant colorectal cancer metastases.

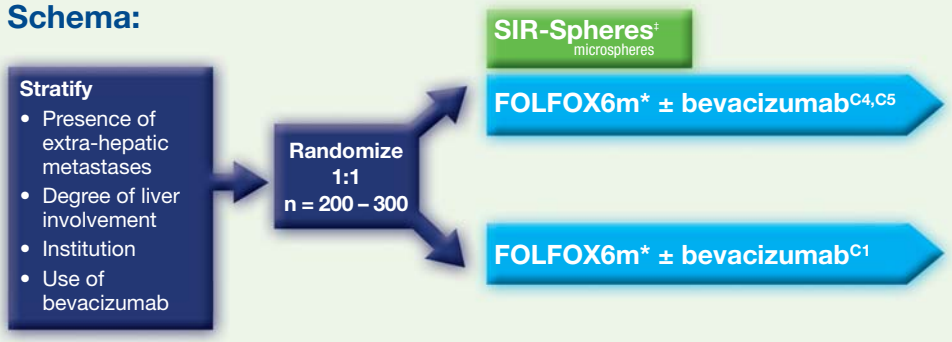
Purpose: To assess the efficacy and safety of adding targeted radiation, in the form of SIR-Spheres microspheres, to a standard-of-care systemic chemotherapy regimen of FOLFOX6m (with or without bevacizumab), compared to FOLFOX6m chemotherapy (with or without bevacizumab) alone as first-line therapy in patients with non-resectable liver metastases from primary colorectal adenocarcinoma, with or without evidence of extra-hepatic metastases. Bevacizumab is allowed at the treating investigator's discretion.

Study Design: Prospective, randomized, open-label, multi-center, multi-national, controlled study.
The study is designed to allow for a combined analysis with clinical data from the SIRFLOX and FOXFIRE studies.

Eligible Patients:

- Unresectable liver-only or liver-predominant colorectal cancer metastases
- No prior chemotherapy for advanced disease
- Fit for combination therapy and selective internal radiation therapy (SIRT)

Schema:



‡ SIR-Spheres microspheres implanted day 3–4 of Cycle 1 or Cycle 2

* Oxaliplatin administered at 60 mg/m2 for 6 weeks in the test arm, starting 3–4 days prior to the SIR-Spheres microspheres administration

C4,C5/C1 At the investigators discretion and relative to the SIR-Spheres microspheres administration date, bevacizumab may commence at Cycle 4 or 5 in the test arm and at Cycle 1 in the control arm

Study Population:	• n = 200 – 300
Primary Endpoint:	• Overall survival (in combination with data from SIRFLOX and FOXFIRE studies)
Secondary Endpoints:	• Progression free survival • Progression free survival in the liver • Objective response rate (liver ± any site) • Health-Related Quality of Life • Liver resection/ablation rate • Safety and tolerability • Health economics

This information concerns a use that has not been approved or cleared by the Food and Drug Administration (FDA). This clinical investigation is being conducted in the USA under an Investigational Device Exemption (IDE) issued by the FDA. SIR-Spheres microspheres are indicated for the treatment of unresectable metastatic liver tumors from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUDR (floxuridine) under a Food and Drug Administration (FDA) approved premarket application (PMA). SIR-Spheres microspheres are approved in Australia, the European Union (CE Mark) and several other countries for the treatment of patients with advanced non-operable liver cancer

Key Inclusion Criteria:

- Histologically confirmed adenocarcinoma of the colon or rectum
- Unequivocal and measurable CT evidence of liver metastases which are not treatable by surgical resection or local ablation with curative intent
- Limited extra-hepatic metastases are allowed:
  - Up to 5 lung metastases ≤ 1 cm or 1 metastasis of ≤ 1.7 cm
  - Lymph nodes < 2 cm in 1 anatomic region (chest, abdomen, pelvis)
- Adequate hematological, renal and hepatic function
- WHO Performance Status 0 – 1
- Life expectancy > 3 months without any active treatment

Key Exclusion Criteria:

- Evidence of ascites, cirrhosis, portal hypertension, main portal venous tumor involvement or thrombosis
- Prior chemotherapy for any malignancy (adjuvant chemotherapy for colorectal cancer is permitted provided that it was completed ≥ 6 months before study entry)
- Concurrent or previous malignancy other than adequately treated non-melanoma skin cancer or carcinoma *in situ* of the cervix
- Previous radiotherapy delivered to the liver
- Peripheral neuropathy > grade 1 (NCI-CTCv3)
- Pregnant or breast feeding

Participating Regions:

• Asia Pacific • Europe • Middle East • Americas

The FOXFIRE Study:

A similar multi-center Phase III randomized controlled trial is being conducted in the UK. This National Cancer Research Institute trial is sponsored by University of Oxford and supported by The Bobby Moore Fund for Cancer Research UK and Sirtex.

The SIRFLOX Study:

Multinational randomized clinical study enrolling a similar population of 518 patients investigating the addition of SIRT with SIR-Spheres microspheres to a standard regimen of FOLFOX6m +/- bevacizumab versus FOLFOX6m +/- bevacizumab alone with a primary endpoint of Progression Free Survival.

For More Information Contact:

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Europe, Middle East and Africa	**info@sirtex-europe.com**
SIRFLOX website	**www.sirflox.com**

This information is intended for clinical investigators and other interested physicians who may wish to enrol or refer patients into this study. Not for distribution to potential or currently enrolled study subjects.

References:

1. Sharma RA *et al.* Radioembolization of liver metastases from colorectal cancer using yttrium-90 microspheres with concomitant systemic oxaliplatin, fluorouracil, and leucovorin chemotherapy. *Journal of Clinical Oncology* 2007; **25**: 1099–1106.
2. Sharma RA *et al.* FOXFIRE: a phase III clinical trial of chemo-radio-embolisation as first-line treatment of liver metastases in patients with colorectal cancer. *Clin Oncol (R Coll Radiol)* 2008; **20**: 261–263.

SIR-Spheres® microspheres

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