

Metastatic colorectal cancer patients treated first-line with SIR-Spheres® Y-90 resin microspheres more likely to become candidates for potentially curative liver surgery, REsect study shows

Surgeons' blinded assessment of pre- and post-treatment CT scans of patients with previously unresectable colorectal cancer liver metastases treated in the SIRFLOX study presented at 12th Annual European-African HPB meeting

Mainz, Germany (24 May 2017) – Adding selective internal radiation therapy (SIRT) with SIR-Spheres Y-90 resin microspheres to first-line FOLFOX-based chemotherapy was associated with a statistically significant gain in potentially curative liver resectability, an independent, international panel of expert liver surgeons has reported.¹

“We performed a blinded evaluation of the extensive radiological database of the recently-reported SIRFLOX study to compare potential liver resectability at baseline and follow-up,” said Dr. Benjamin Garlipp, the principal author of the REsect study and a liver surgeon at Otto-von-Guericke-Universität, Magdeburg, Germany. “We found that while resectability increased from baseline to follow-up in both the chemotherapy only arm and the chemotherapy + SIRT arm of the SIRFLOX study, the increase was significantly more pronounced in patients receiving the combination treatment – 38.1% of these were resectable on the basis of their liver CT scan at follow-up, compared to 28.9% of the patients receiving chemotherapy only ($p < 0.0001$). This is an important finding because surgical resection is the mainstay of potentially curative treatments for these patients, and there is an increasing body of evidence suggesting that it can prolong their lives even though most of them eventually recur.”

Of the 472 SIRFLOX study patients whose pre- and post-treatment liver CT scans were evaluable by the REsect surgeons, 228 had received first-line mFOLFOX6 chemotherapy (\pm bevacizumab), while 244 were treated with the combination of chemotherapy and SIR-Spheres Y-90 resin microspheres.^{1,2} There was no significant difference in the resectability of the patients' liver metastases at baseline (11.0% vs. 11.9%; $p = 0.775$). In a second analysis, of the patients who were deemed still unresectable at baseline, significantly more patients in the Y-90 resin microspheres group had resectable liver metastases compared to those who received chemotherapy alone (31.2% vs. 22.7%; $p < 0.0001$).¹

The REsect study was conducted by a panel of 14 HPB (Hepato-Pancreato-Biliary) surgeons from leading medical centres in Belgium, France, Germany, Italy, The Netherlands, Spain, the UK and the USA.¹ Five surgeons performed independent, blinded analyses of 100 baseline and follow-up scans chosen at random from the 472 cases to be reviewed. Blinded analysis of the remaining scans was conducted of 22–25 cases at a time by three surgeons working independently and chosen at random from the nine other members of the REsect panel. The reviewers were blinded to patient identifiers, visit (baseline or follow-up), treatment and clinical information, as well as being blinded to the other

reviewers' assessments. A patient was deemed to be resectable or unresectable by majority agreement (≥ 3 of 5 surgeons or ≥ 2 of 3 surgeons).

"As a surgeon, it is always my aim to offer the option of a potentially curative liver resection to patients with mCRC. We know that in many patients with metastatic colorectal cancer the liver is the only organ with cancer deposits, and converting patients from a stage where resection of the disease is not possible into one where potential curative resection becomes an option again has an enormous impact for patients. This retrospective analysis suggests that SIRT with Y-90 resin microspheres could be a means to achieving resection for more of these patients," Dr Garlipp emphasized.

What is SIRT with SIR-Spheres Y-90 resin microspheres?

SIRT with SIR-Spheres Y-90 resin microspheres is an approved treatment for inoperable liver tumours. It is a minimally-invasive treatment that delivers high doses of high-energy beta radiation directly to the tumours. SIRT is administered to patients by interventional radiologists, who infuse millions of radioactive resin microspheres (diameter between 20–60 microns) via a catheter into the liver arteries that supply blood to the tumours. By using the tumours' blood supply, the microspheres selectively target liver tumours with a dose of radiation that is up to 40 times higher than conventional radiotherapy, while sparing healthy tissue.

SIR-Spheres Y-90 resin microspheres are approved for use in Argentina, Australia, Brazil, the European Union (CE Mark), Switzerland, Turkey, and several countries in Asia for the treatment of unresectable liver tumours. In the US, SIR-Spheres Y-90 resin microspheres have a Pre-Market Approval (PMA) from the FDA and are indicated for the treatment of unresectable metastatic liver tumours from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUDR (floxuridine).

About Sirtex

Sirtex Medical Limited (ASX: SRX) is an Australian-based global healthcare business working to improve treatment outcomes in people with cancer. Our current lead product is a targeted radiation therapy for liver cancer called SIR-Spheres Y-90 resin microspheres. Approximately 73,000 doses have been supplied to treat patients with liver cancer at more than 1060 medical centres in over 40 countries. For more information, please visit www.sirtex.com.

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2. van Hazel GA *et al.* SIRFLOX: Randomized phase III trial comparing first-line mFOLFOX6 (plus or minus bevacizumab) versus mFOLFOX6 (plus or minus bevacizumab) plus selective internal radiation therapy in patients with metastatic colorectal cancer. *J Clin Oncol* 2016; **34**: 1723–1731.

689-EUA-0517