



Multi-centre Phase II Trial Reports Safety and Clinical Benefits of Radioactive Microspheres in Patients with Colorectal Cancer Liver Metastases who have Failed Chemotherapy

Rome – 19 August 2010 – Radioactive yttrium-90 labelled resin microspheres (SIR-Spheres; Sirtex Medical, Sydney, Australia) appear to be a safe and effective treatment for patients with colorectal cancer liver metastases who have failed available chemotherapy options, according to the final results of a prospective clinical multi-centre phase II trial conducted by the Italian Society of Locoregional Therapies in Oncology (SITIO) and published in the *British Journal of Cancer*.¹

The results of the 52-patient study revealed that the liver tumours completely disappeared in one patient (2%), and 11 (22%) patients had a partial response involving at least a 30% reduction in tumour size, which met the pre-determined criteria for significance ($P = 0.05$). A further 12 (24%) patients had stable disease. The liver tumours shrank sufficiently in two patients (4%) to enable potentially curative surgery to be performed. The median overall survival was 12.6 months for all patients in the trial, with significantly longer survival in the 24 (48%) patients that responded to SIR-Spheres or who had stable disease compared to non-responders (median 16 months versus 8 months; $P = 0.0006$), and 40% of the responders remaining alive at two years compared to none of the non-responders. Mild-to-moderate side effects consisting mostly of fever and pain were reported in 16% of patients in the first 48 hours and 22% in days 3 to 30.

“These results reveal that radioembolisation using SIR-Spheres is a promising therapy for patients with colorectal cancer liver metastases who have failed chemotherapy,” said Prof. Maurizio Cosimelli, Professor of Surgery at the Regina Elena National Cancer Institute in Rome, and co-ordinator of the study. “The prolonged 12.6-month median survival and encouraging tumour response reported in the SITIO study compares favourably with the clinical trial results of second- or third-line chemotherapy, even though three-quarters of our patients had previously received at least four different combinations of chemotherapy drugs and therefore had a poor prognosis with no other treatment options available.”

“At a minimum, patients with liver-only or liver-dominant colorectal cancer who are failing chemotherapy and who remain fit should be considered for radioembolisation using SIR-Spheres,” said Prof. Cosimelli. “However, SITIO will be conducting a multi-centre randomised trial using SIR-Spheres in combination with chemotherapy at an earlier line of treatment since we believe that this may further improve the prognosis for patients with colorectal liver metastases. Above all, it will be possible to clarify the potential of SIRT together with chemotherapy to increase the rate of surgical resections in patients that were previously unresectable”

Patients in the SITIO study had to have liver metastases from colorectal cancer that could not be removed by surgery and which had progressed despite modern chemotherapy regimens containing oxaliplatin and irinotecan. The presence of metastases outside the liver did not exclude the patients from treatment as long as these were limited in number, size and in the same organ. All patients were heavily pre-treated, having received at least 3 previous chemotherapy regimens: 24% had received 3 different lines or courses of chemotherapy, 50% had received 4 lines and 26% had received 5 lines.

The SITIO study used a single-arm design since this group of patients had no other treatment options available. Patients were reviewed by a multidisciplinary team of cancer specialists prior to recruitment into the study. The median survival of metastatic colorectal cancer treated in clinical

studies using modern chemotherapy regimens such as cetuximab plus irinotecan at second-line and panitumumab at third-line treatment has been reported to be 8.6 to 10.7 months²⁻⁵ and 6.3 to 9.3 months⁶⁻⁹ respectively.

Each year, more than 145,000 Americans and 307,000 Europeans are diagnosed with colorectal cancer. Around half of these patients will develop metastases that have spread from the original site of the disease, predominately to the liver. Up to 90% of these patients ultimately die from liver failure due to the spread of the disease. Selective Internal Radiation Therapy (SIRT) using ⁹⁰Y microsphere therapy is a novel approach to treating liver metastases. The microspheres are implanted by interventional radiologists to selectively target the tumors with radiation while sparing the much-needed healthy liver tissue.

The SITILO study was conducted by a multidisciplinary team of interventional radiologists, nuclear medicine physicians, medical oncologists, surgeons and other specialists at the Regina Elena National Cancer Institute in Rome, the University of Bologna, the University of Udine and the Cancer Institute of Naples in Italy. SIR-Spheres was developed by and is manufactured by Sirtex Medical, and is the only FDA-approved microsphere therapy for colorectal cancer liver metastases.

SITILO is the only Italian multidisciplinary oncology society. Different specialties work together within SITILO to design prospective clinical trials on loco-regional therapies in the field of liver metastases and primary carcinoma, melanoma, soft tissue sarcoma, and other cancers. Each protocol includes a biological component aimed at identifying predictive factors in serum and tissue.

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The SITILO trial was conducted at the following hospitals:

- Regina Elena Cancer Institute, Rome, Italy
- University of Bologna, Bologna, Italy
- University of Udine, Udine, Italy
- Fondazione Pascale Cancer Institute, Naples, Italy

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