



**Final Results of Clinical Trial Combining SIR-Spheres[®] microspheres with Chemotherapy
in Patients with Inoperable Liver Metastases from Colorectal Cancer
Published in Journal of Clinical Oncology**

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Australian-based biotechnology and medical device company Sirtex Medical Limited (SRX) is pleased to announce the publication in the *Journal of Clinical Oncology*¹ of the final results of a clinical trial of the use of SIR-Spheres[®] microspheres in combination with modern oxaliplatin-based chemotherapy to treat patients with inoperable liver metastases from colorectal cancer.

The non-randomised dose escalation trial was designed to assess the safety and toxicity of combining selective internal radiation therapy (SIRT), using SIR-Spheres microspheres, with FOLFOX4², a standard-of-care chemotherapy regimen typically used for the first-line treatment of metastatic colorectal cancer.

This is the first study of SIRT in combination with a chemotherapy regimen that incorporates oxaliplatin, which is known to sensitise tumours to the effects of radiation therapy.

Twenty patients with inoperable liver metastases from colorectal cancer who had not previously received chemotherapy for metastatic disease were enrolled in the study in Australia and the United Kingdom³.

While acknowledging the small sample size, the investigators concluded that the combination treatment was generally well-tolerated by the patient group, and noted that the lack of liver toxicity was encouraging for the clinical advancement of a multimodality treatment approach.

They also concluded that the patient outcomes are impressive when compared to equivalent statistics for FOLFOX4 chemotherapy alone, in this patient group.

Of the 20 patients in the study, 18 (90%) showed a decrease in the tumour size by at least 30 per cent according to RECIST⁴ criteria and two patients (10%) had stabilisation of their disease.

The tumours decreased in size sufficiently in two patients (10%) to enable their remaining liver tumours to be removed by surgery.

Median progression-free survival was 9.3 months (range 3.9 to 30.7 months), and median time to progression in the liver was 12.3 months (range 6.3 to 24.9 months). In the subset of seven patients with metastases in the liver only, median progression-free survival was 14.2 months.

The investigators determined the doses of FOLFOX4 that should be used in future clinical trials with SIR-Spheres microspheres, and they concluded that the chemoradiation regimen of FOLFOX4 plus SIRT merits further evaluation in larger phase 2 and phase 3 trials.

An expanded randomised controlled study comparing the efficacy of FOLFOX6 chemotherapy plus SIR-Spheres microspheres versus FOLFOX6 chemotherapy alone is currently being conducted in Australia (as previously announced to ASX 27/09/06) and has received US FDA approval to be conducted in US under IDE. This trial will further study patients with inoperable colorectal liver metastases who have not previously received chemotherapy for the spread of their disease.

About Selective Internal Radiation Therapy (SIRT) using SIR-Spheres microspheres

Selective Internal Radiation Therapy (SIRT) is a novel treatment for inoperable liver cancer that delivers high doses of radiation directly to the site of tumours. In a minimally invasive treatment, millions of radioactive SIR-Spheres microspheres are infused via a catheter into the liver where they selectively target liver tumours with a dose of internal radiation up to 40 times higher than conventional radiotherapy, while sparing healthy tissue.

Clinical trials have confirmed that liver cancer patients treated with SIR-Spheres microspheres have response rates higher than with other forms of treatment, resulting in increased life expectancy, greater periods without tumour activity, and improved quality of life. SIRT has been found to shrink liver tumours more than chemotherapy alone.

SIRT using SIR-Spheres microspheres is approved for use in Australia, New Zealand, the United States of America (FDA approval), European Union (CE Mark), Hong Kong, Malaysia, Singapore, Thailand, Israel, and India. SIRT is available in 140 treatment centres around the world, and more than 6500 patients have been treated to date.

About Liver Cancer

Liver cancer is the biggest cancer-related killer of adults in the world. Each year, more than 500,000 new cases of primary liver cancer develop worldwide and at least 200,000 new cases of secondary liver cancer develop from primary bowel cancer alone. It is estimated that secondary liver cancer is the ultimate cause of death for one in three cancer sufferers. Liver tumours are inoperable in 90 per cent of cases, and are typically incurable with chemotherapy.

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For more information, visit our website at www.sirtex.com

Contact: Gilman Wong, CEO, +61-2-9936-1400

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¹ Sharma R, van Hazel G, Morgan B *et al.* Radioembolization of liver metastases from colorectal cancer using yttrium-90 microspheres with concomitant systemic oxaliplatin, fluorouracil, and leucovorin chemotherapy. *J Clin Oncol* 2007; **25**: 1099–1106.

² The 'FOLFOX4' chemotherapy schedule used in this study included 12 cycles of oxaliplatin, 5-fluorouracil (5FU) and leucovorin (LV), with the oxaliplatin dose for the first 3 cycles being escalated from 30 mg/m² to the normal dose of 85 mg/m² after safety in the previous dose group had been established. Selective internal radiation therapy or radioembolisation using SIR-Spheres microspheres was given on day 3 or 4 of the first cycle of chemotherapy.

³ The SIRT plus FOLFOX chemotherapy study was conducted at the following hospitals:

- University Hospitals of Leicester, Leicester, UK
- Perth Oncology, Mount Medical Centre, Perth, Australia
- Nepean Hospital, Sydney, Australia
- Epworth Hospital, Melbourne, Australia

⁴ Response Evaluation Criteria in Solid Tumours (partial response = greater than 30% reduction)