



Press Release

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Studies Reconfirm Significant Benefits Regarding the Use of SIR-Spheres® Microspheres for the Treatment of Inoperable Liver Tumors

Sirtex Announces Latest Clinical Findings and Provides Updates on Research Initiatives

WILMINGTON, Mass. (November 30, 2010) — [Sirtex](#), a leading developer of targeted and innovative liver cancer therapies, provided an update on clinical initiatives regarding SIR-Spheres® microspheres. Highlights include the results of two independent studies in Belgium and Italy published recently in the *Journal of Clinical Oncology* and the *British Journal of Cancer*, respectively. The studies reconfirmed evidence from earlier research that established “significant clinical benefits from the use of targeted radioactive SIR-Spheres microspheres as an effective option for patients with inoperable liver cancer.”

In addition to the two completed studies, Sirtex also released updates regarding a larger, independent global study currently enrolling patients at 40 sites including several in the United States. The SIRFLOX study, with a primary endpoint of Progression Free Survival, is a prospective randomized study looking at SIR-Spheres microspheres in combination with chemotherapy for first line treatment of patients with unresectable liver metastases from colorectal cancer.

Belgian Study Yields Positive Results for Patients with Metastatic Colon Cancer

Results of a randomized controlled 46-patient Belgian trial published in the *Journal of Clinical Oncology* revealed that in patients with liver metastases from colorectal cancer who had failed all available standard-of-care chemotherapy, SIR-Spheres microspheres more than doubled the time to progression in the liver (the primary endpoint of the study) from a median of 2.1 months in patients receiving chemotherapy alone to 5.5 months in patients receiving SIR-Spheres microspheres plus chemotherapy (p=0.003).^{1,2}

SIR-Spheres microspheres also significantly extended the time to progression of disease anywhere in the body, from 2.1 months in the chemotherapy control arm to 4.5 months in patients in the combination arm (p=0.03), as well as significantly increasing disease control, from 35 percent to 85 percent, respectively (p=0.001).

For ethical reasons, the trial included a cross-over design for patients in the control arm following failure of chemotherapy alone. All patients in the control arm were reassessed for suitability for SIR-Spheres microspheres, with 43 percent of patients receiving Selective Internal Radiation Therapy (SIRT).

Median survival increased from 7.3 months in the chemotherapy control arm to 10 months in the SIR-Spheres microspheres plus chemotherapy arm.

Investigators noted that SIR-Spheres microspheres should be considered as a valid therapeutic option for patients with chemotherapy-refractory liver-limited metastatic colorectal cancer (mCRC).

Italian Multi-Center Study Produces Significant Response in Patients

At the same time, the results of a 50-patient, independent, multi-center Italian study published in the *British Journal of Cancer* showed SIR-Spheres microspheres produced a significant and meaningful response in patients with advanced inoperable liver tumors who had failed all available chemotherapy treatments.^{3,4} The study, conducted by the Italian Society of Locoregional Therapies in Oncology (SITILO), was the first single-arm, prospective clinical trial of SIR-Spheres microspheres in the salvage therapy of patients with mCRC who had been heavily pre-treated with chemotherapy.

The results revealed an overall response rate of 24 percent, which met the trial's pre-determined criteria for significance, plus stable disease reported in a further 24 percent of patients.

In two patients, the tumors shrank sufficiently to permit surgeons to plan potentially curative surgery. The median overall survival for the trial was 12.6 months. Patients that responded to SIR-Spheres microspheres, or who had stable disease, experienced a significantly longer median survival compared to non-responders (16 months versus 8 months; $p=0.0006$), with 40 percent of the responders remaining alive at two years compared to none of the non-responders.

The investigators concluded that patients with liver-only or liver-dominant colorectal cancer metastases who had failed chemotherapy and who remained fit should be considered for radioembolization, which highlights the potential for SIR-Spheres microspheres to be used to provide meaningful clinical benefits in a greater number of patients than at present.

SIRFLOX Study Currently Enrolling

SIRFLOX is the first prospective randomized study looking at SIR-Spheres microspheres in combination with standard therapy for first line treatment, FOLFOX6 with or without bevacizumab, in patients with unresectable liver metastases from colorectal cancer. The primary endpoint of the study is Progression Free Survival.

The SIRFLOX study is open and enrolling at more than 40 sites worldwide. To date, 180 patients have enrolled with enrollment of 450 patients anticipated complete by the end of 2011. An independent data safety monitoring committee (IDSMC) recently finalized a safety analysis on the first 80 patients and found the study has no major safety issues that would preclude continuing as scheduled.

The aim of SIRFLOX is to determine if SIR-Spheres microspheres in combination with FOLFOX6 with or without bevacizumab can be considered a valid first line option for patients with liver-limited metastatic colorectal cancer.

A sister study, FOXFIRE, is underway in the United Kingdom. The study is identical in design except that the primary endpoint is Overall Survival. It is anticipated that data on over 800 patients from the two trials can be combined to determine an Overall Survival endpoint across both studies.

“These two independent studies provide further evidence that SIR-Spheres microspheres can improve clinical outcomes in a patient population with limited treatment options,” said Michael Mangano, President, Sirtex Medical Inc. “We are excited that the SIRFLOX trial is well underway in the United States. We believe that this study, along with FOXFIRE, will confirm that SIR-Spheres microspheres should be added to modern first-line chemotherapy for patients with metastatic colorectal cancer, to extend survival, in line with the clinical benefits seen in the two European studies in patients who have failed all available treatment options.”

SIR-Spheres microspheres therapy is available to patients throughout the United States and a full list of treating sites can be found at www.sirtex.com. For more information on the SIRFLOX study, please visit www.sirflox.com/home.

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

Selective Internal Radiation Therapy (SIRT), also known as radioembolization, is a novel treatment for inoperable liver cancer that delivers high doses of radiation directly to the site of tumors. In a minimally-invasive treatment, millions of radioactive SIR-Spheres microspheres are infused via a catheter into the liver where they selectively target liver tumors 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 tumor activity, and improved quality of life. SIRT has been found to shrink liver tumors more than chemotherapy alone.

SIR-Spheres microspheres are approved for use in Australia, the United States of America (FDA approval), and the European Union (CE Mark) and additionally supplied in countries such as Hong Kong, Malaysia, Singapore, Thailand, Taiwan, India, Israel and Turkey with approximately 13,500 treatments worldwide.

Manufactured by Sirtex, SIR-Spheres microspheres are the only FDA-approved microsphere radiation therapy for the treatment of colorectal liver metastases. Sirtex Medical Inc.'s SIR-Spheres microspheres are indicated for the treatment of non-resectable metastatic colorectal cancer in combination with intra-arterial FUDR chemotherapy. Information regarding other disease states or agents in combination with this device, that is presented in peer-reviewed literature or medical meetings may differ from the approved USA indications as per the labeling for the product.

1. Hendlisz A, Van den Eynde M, Peeters M *et al.* Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard chemotherapy. *Journal of Clinical Oncology* 2010; 28: 3687–3694.

2. The clinical trial was conducted at the following university hospitals:

- Institut Jules Bordet, Brussels, Belgium
- Universitair Ziekenhuis Gent, Gent, Belgium
- University Hospital Gasthuisberg, Leuven, Belgium

3. Cosimelli M, Golfieri R, Cagol PP *et al.* Multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases. *British Journal of Cancer* 2010; 103: 324–331.

4. The SITILO clinical 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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