

SIRFLOX Study Presented at ASCO 2015 Annual Meeting



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CHICAGO, May 30, 2015 /PRNewswire/ --

Clinical investigators cite significance of 7.9 month improvement in Progression-Free Survival in the liver for patients with unresectable metastatic colorectal cancer (mCRC) treated first line with SIR-Spheres® Y-90 resin microspheres plus chemotherapy

The benefits of adding liver-directed SIR-Spheres Y-90 resin microspheres to a current systemic chemotherapy for the first-line treatment of unresectable metastatic colorectal cancer (mCRC) reported in the SIRFLOX study, were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. The results of the 530-patient SIRFLOX randomized controlled study, which open new possibilities

for combining radiation targeted at liver metastases with first-line systemic treatment of mCRC, were presented by Associate Professor Peter Gibbs, co-principal investigator of the SIRFLOX study and Consultant Medical Oncologist, The Royal Melbourne Hospital, Australia.

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"We found that while liver tumours began to grow again after a median of 12.6 months in patients with mCRC who received only first-line chemotherapy, those who also received first-line treatment with SIR-Spheres Y-90 resin microspheres had their liver tumours controlled for a median of 20.5 months. The additional 7.9 months of treatment benefit with the combined first-line SIRFLOX regimen was statistically significant, with a p-value of 0.002 and a hazard ratio of 0.69. This translates to a 31 percent reduction in the risk of tumour progression in the liver for patients treated with Y-90 resin microspheres," Prof. Gibbs said.

"This finding matters a great deal," he explained, "because the liver is almost invariably the organ where colorectal cancer spreads to first. While half the patients initially diagnosed with colorectal cancer survive thanks to surgical removal of the primary tumour before the disease has spread elsewhere in the body, liver metastases eventually cause the death of the majority of the remaining hundreds of thousands of patients each year whose tumours spread but are inoperable."

Prof. Gibbs also told the ASCO audience that liver treatment response rates were significantly higher in patients who received Y-90 resin microspheres in combination with first-line chemotherapy, which consisted of a FOLFOX-based regimen, with or without the addition of bevacizumab. "We observed a hepatic response rate of 78.7 percent in this group, compared to 68.8 percent in the chemotherapy-only group. This was statistically significant, with a p-value of 0.042. Moreover, the rate of complete responses in the liver of SIRFLOX patients who received SIR-Spheres Y-90 resin microspheres, though relatively small at 6.0 percent, was more than three times higher than the 1.9 percent complete response rate among the chemotherapy-only patients. The statistical significance of this finding is very strong, with a p-value of 0.02," Prof. Gibbs stated.

Other SIRFLOX Clinical Investigators Discuss Study Implications

At a press conference following Prof. Gibbs's SIRFLOX presentation, Prof. Guy van Hazel, co-principal investigator of SIRFLOX and Clinical Professor of Medicine at the University of Western Australia, Perth, said that "SIRFLOX gives us the data to validate the first-line use of selective internal radiation therapy, or SIRT, with SIR-Spheres Y-90 resin microspheres in mCRC. Until now, we have not had a randomized clinical study large enough to provide Level One evidence supporting first-line use of this treatment."

"This step forward matters to medical oncologists and their patients, because until the development of Y-90 resin microspheres, there was essentially no place for radiation therapy in the treatment of liver tumours. There was never a question that radiation would work in the liver, but the problem of administering the radiation in a way that spared healthy liver tissue from its effects prevented it from being an 'equal partner' with surgery and chemotherapy in treating mCRC, as it is in almost all other forms of cancer," Prof. van Hazel added.

The principal European investigator of SIRFLOX, Prof. Volker Heinemann, Director of the Comprehensive Cancer Center at the University of Munich, Germany, told the press conference audience that, "Medical oncologists, particularly also at the community level, are only now beginning to recognize that treating liver

metastases locally as well as systemically is a very important clinical consideration in the effective management of this difficult-to-treat cancer, and may also open up the possibility of potentially curative liver surgery in some previously unresectable cases."

"The effect of Y-90 resin microspheres on Progression-Free Survival in the liver, as reported in the SIRFLOX study, is quite pronounced," Prof. Heinemann continued. "Even in the absence of sufficient data to calculate an overall survival benefit or a significant finding for the primary endpoint of Progression-Free Survival at any site, the outcome of SIRFLOX suggests that oncologists who treat mCRC may now wish to consider earlier use of Y-90 resin microspheres than is presently the case, certainly among those patients whose metastatic disease has been diagnosed primarily in the liver."

"With SIRFLOX, the Level One evidence is there for every medical oncologist to see and to evaluate in their practice," he said.

The principal U.S. investigator of SIRFLOX, Dr. Navesh K. Sharma, Assistant Professor of Radiation Oncology and Diagnostic/Interventional Radiology at the University of Maryland Medical Center, which was the largest US clinical site for SIRFLOX, said that, "With 530 patients, SIRFLOX is the largest randomized trial ever conducted that combined an interventional radiology procedure with chemotherapy in oncology."

"Physicians have been performing SIRT procedures with Y-90 resin microspheres, in the US and around the world, for more than 10 years. We have always felt that this procedure was a unique approach to deliver large doses of radiation to liver tumours, targeted in a way that spares healthy liver tissue. It is important to observe that in SIRFLOX, the clinical benefit that was observed came with an acceptable level of adverse events from adding Y-90 resin microspheres to first-line chemotherapy in mCRC. Oncologists, especially radiation oncologists, have traditionally been very cautious of irradiating large liver volumes because of the adverse effects associated with such treatments. SIRFLOX has shown us, in an unbiased manner that not only can we deliver high doses of radiation to the liver safely with this approach, but we can do so using concurrent chemotherapy. Concurrent chemo-radiation has been one of the most effective ways to treat cancer in general, especially those of gastrointestinal origin," Dr. Sharma said.

In a further indication of the potential clinical relevance of the combined chemo-radiation regimen studied in SIRFLOX, ASCO has selected the SIRFLOX study results as one of just 71 of the several thousand abstracts reviewed for this meeting as a "Best of ASCO" presentation. "Best of ASCO" papers may be discussed in an ongoing cascade of official follow-up presentations that national oncology leaders will deliver over the coming months to medical oncologists in their countries who were unable to attend the ASCO Congress in Chicago.

SIRFLOX is the first of a group of three studies assessing the results of adding SIR-Spheres Y-90 resin microspheres to first-line chemotherapy in the treatment of mCRC. The other studies are FOXFIRE, a UK clinical trial that completed enrolment in November 2014, and FOXFIRE Global, an international study that completed enrolment in January 2015. The results of the three studies, which together enrolled more than 1,100 mCRC patients, will be combined in a pre-planned assessment of the overall survival benefit of adding SIR-Spheres Y-90 resin microspheres to first-line chemotherapy for mCRC. The combined results are expected in 2017.

The co-principal investigators of FOXFIRE are Professor Ricky Sharma, Clinical Senior Lecturer in Oncology at the University of Oxford, UK, and Dr. Harpreet Wasan of Hammersmith Hospital and the Imperial College Trust, London, UK. Professor Sharma was also the discussant of SIRFLOX at the ASCO Annual Meeting in Chicago. Professor Peter Gibbs is the principal investigator of FOXFIRE Global.

About SIR-Spheres Y-90 Resin Microspheres

SIR-Spheres Y-90 resin microspheres are a medical device used in an interventional radiology procedure known as selective internal radiation (SIRT), or radioembolisation, which targets high doses of radiation directly to liver tumours. The treatment consists of tens of millions of radioactive Y-90 coated resin particles, each no bigger in diameter than a human hair. Interventional radiologists inject these resin particles, or microspheres, into the hepatic artery via a catheter inserted into the femoral artery through an incision in the groin. The Y-90 resin microspheres become lodged in the capillaries that surround liver tumours, where they deliver a high dose of short-range (mean 2.5 mm; maximum 11 mm) beta radiation to the liver tumours, while sparing healthy liver tissue. The low specific gravity of Y-90 resin microspheres allows the blood flow to evenly distribute the radioactivity within and around the liver tumours.

Key SIR-Spheres Y-90 resin microspheres regulatory authorisations include a full Pre-Market Approval from the US FDA, European Union (CE Mark) and Australian TGA Conformity Assessment certification.

SIR-Spheres Y-90 resin microspheres also have a Premarket Approval (PMA) by the FDA and are indicated in the United States for the treatment of non-resectable metastatic liver tumors from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine. SIR-Spheres Y-90 resin microspheres are approved for the treatment of inoperable liver tumors in Australia, the European Union (CE Mark), Argentina (ANMAT), Brazil, and several countries in Asia, such as India and Singapore.

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 50,000 doses have been supplied to treat patients with liver cancer at more than 800 medical centres in over 40 countries.

For more information, please visit <http://www.sirtex.com> (<http://www.sirtex.com>).

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Reference:

Gibbs P *et al.* 2015 ASCO Annual Meeting; *J Clin Oncol* 2015; **33** (Suppl): Abs 3502.

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