



New European Society of Medical Oncology (ESMO) Biliary Cancer Guidelines Indicate Selective Internal Radiation Therapy (SIRT) with Y-90 Microspheres as an Option for Post-Chemotherapy Treatment of Intrahepatic Cholangiocarcinoma (iCCA)

Sydney, Australia (11 October 2016)

Sirtex Medical Limited (ASX:SRX) announced today that the European Society of Medical Oncology (ESMO) has indicated the use of SIRT using yttrium-90 (Y-90) microspheres as an option for the treatment of intrahepatic cholangiocarcinoma (iCCA), a form of primary liver cancer that starts in the bile duct, the branching network of thin tubes that deliver fat-digesting bile from the liver to the small intestine.¹

The new ESMO guidelines on biliary cancers were published in September 2016 as a supplement to the *Annals of Oncology*.¹ Their lead author, Professor Juan Valle, department of medical oncology, Christie NHS Foundation Trust, University of Manchester, UK, states that selective internal radiation therapy (SIRT), which is also known as radioembolisation, “may be considered in patients with inoperable iCCA, usually after first-line chemotherapy.”

The ESMO inclusion of SIRT for the treatment of iCCA was based on ESMO’s review of a pooled analysis of 12 studies totalling 298 patients that was published in the *European Journal of Surgical Oncology* in 2015, by Dr D. P. Al-Adra of the University of Edmonton, Canada and others.² These data showed a median overall survival of 15.5 months and treatment response rate of 28% in patients treated with SIRT.

In addition, the new ESMO guidelines on biliary cancers call special attention to a subset of studies in the pooled SIRT analysis, stating that “importantly, 7/73 (10%) patients in three selected studies were converted to resectable disease, highlighting the importance of reassessment of patients in the multidisciplinary team in the event of a good response to any treatment.”

Dr David N. Cade, Chief Medical Officer of Sirtex Medical Limited, said that “We are delighted to see SIR-Spheres® Y-90 resin microspheres cited in the new ESMO guidelines as an important post-chemotherapy option for patients with locally advanced or metastatic iCCA, given no current standard of care exists beyond first-line treatment with cisplatin and gemcitabine chemotherapy in these patients. We believe that these are the first international clinical guidelines to indicate SIRT as a treatment option for patients with iCCA.”

Most iCCA patients are diagnosed relatively late in the course of their disease, and therefore are not immediately eligible for potentially curative surgical resection. The fact that even a small proportion of these patients may become surgically resectable suggests that SIRT may offer real hope for them.

Dr Cade added that, “The relatively favourable outcomes for iCCA patients treated using SIR-Spheres Y-90 resin microspheres after having already failed chemotherapy have encouraged Sirtex to conduct a randomised controlled study in the setting of first-line treatment for iCCA. The SIRT in Cholangiocarcinoma (SIRCCA) study is examining the role of SIR-Spheres Y-90 resin microspheres followed by the standard-of-care first-line chemotherapy for iCCA, compared to chemotherapy alone.

SIRCCA is being conducted in some 30 centres in Australia and several European countries, including Belgium, France, Germany, Italy, Spain, The Netherlands and UK.

About Cholangiocarcinoma

Although relatively rare, cholangiocarcinoma is the second-most common form of primary liver cancer.³ The most common form of primary liver cancer, HCC or hepatocellular carcinoma, is the world’s second-largest cause of cancer deaths.⁴

In the westernized countries of Europe, North America and Australasia, incidence rates are low, with estimates ranging from 0.3 to 3.5 cases per 100,000 people annually. However, incidence rates are much higher in parts of the world where parasitic liver fluke infections are common, which includes Thailand, China and Korea. Northeast Thailand has the highest rate of cholangiocarcinoma in the world, 90 cases per 100,000 people each year.¹

Other than liver fluke infection, cholangiocarcinoma can be caused by chronic damage to the liver or bile duct, such as chronic inflammation (primary sclerosing cholangitis, or PSC), bile-filled choledochal cysts and bile duct stones.⁵

Surgical resection of the cancerous tissue can represent a definitive cure for cholangiocarcinoma that is diagnosed early. For those patients diagnosed with later-stage disease, chemotherapy with cisplatin and gemcitabine (a combination referred to as CIS-GEM) is the initial treatment of choice, with SIRT now regarded as an option for the next line of therapy.

The intrahepatic form of cholangiocarcinoma (iCCA) covered in the new ESMO guideline is one of three types of the disease that physicians differentiate, primarily based on where the disease is located within the target organ. The other two forms are perihilar cholangiocarcinoma (pCCA), and distal cholangiocarcinoma (dCCA).¹

About The Selective Internal Radiation Therapy in Cholangiocarcinoma (SIRCCA) Study

SIRCCA, which will begin recruiting patients in late 2016, is a randomised clinical study for patients with intrahepatic cholangiocarcinoma (iCCA), a form of primary liver cancer that originates in the bile duct, a branching network of thin tubes that start in the segments of the liver and deliver fat-digesting bile to the small intestine. The SIRCCA study, sponsored by Sirtex, is designed to compare the effects of treating iCCA patients using the sequence of SIR-Spheres Y-90 resin microspheres followed by the standard-of-care cisplatin plus gemcitabine (CIS-GEM) chemotherapy versus CIS-GEM chemotherapy alone.

The key eligibility patient criteria are unresectable intrahepatic cholangiocarcinoma that is confined to the liver or predominately in the liver, who have not previously received chemotherapy, with adequate blood, liver and kidney function, and in good overall health

(defined as ECOG performance status 0 or 1; ECOG 0 is fully active, while ECOG 1 is restricted in physically strenuous activity but able to carry out light house work or office work).

SIRCCA will enroll 180 patients at more than 30 treatment centres in, Australia and several European countries, including Belgium, France, Germany, Italy, Spain, The Netherlands and UK. The principal investigators of SIRCCA are Dr Harpreet Wasan, Hammersmith Hospital, Imperial College, London UK and Prof. Jordi Bruix, Barcelona Clinic, Spain. More information about SIRCCA can be found at <https://clinicaltrials.gov/ct2/show/NCT02807181>.

About SIRT

Selective Internal Radiation Therapy (SIRT), also known as radioembolisation, is a liver-directed therapy for inoperable liver tumours, which is why the new ESMO guideline specifies its use for cholangiocarcinoma within the liver.¹ SIRT is administered by a specially trained Interventional Radiologist. A microcatheter is used to deliver millions of radioactive microspheres into the hepatic artery, where they are carried into the arterioles and selectively lodge in the tumour microvasculature.

About SIR-Spheres Y-90 resin microspheres

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 tumors 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, SIR-Spheres Y-90 resin microspheres, is a targeted radiation therapy for liver cancer. Approximately 67,000 doses have been supplied to treat patients with liver cancer at more than 1,000 medical centres in over 40 countries. For more information, please visit www.sirtex.com.

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