SIRTEX MEDICAL LIMITED (ASX: SRX)

An emerging global leader in cancer treatment

Sirtex is a global life-sciences company that develops and delivers oncology treatments using novel small particle technology to help improve outcomes for patients with cancer.

Extending the lives of patients with SIR-Spheres® Y-90 resin microspheres

Sirtex's lead product is an internal radiation therapy called SIR-Spheres Y-90 resin microspheres that targets high doses of radiation to primary and secondary liver tumours via the hepatic artery. This involves a minimally invasive procedure called Selective Internal Radiation Therapy (SIRT). SIR-Spheres Y-90 resin microspheres are approved in Australia, the European Union (CE Mark), and several other countries in- and outside Asia for the treatment of patients with advanced non-resectable liver tumours. In the USA, SIR-Spheres Y-90 resin microspheres have a full Pre-Market Approval (PMA) from the Food and Drug Administration (FDA) and are indicated for the treatment of unresectable metastatic liver tumours from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUDR (Floxuridine).

SIR-Spheres Y-90 resin microspheres are tiny radioactive resin beads that emit radiation and possess unique physical characteristics and biological effects.[1] They are only about one third the width of a human hair and have about the same specific gravity as a red blood cell. This enables the microspheres to flow easily in the blood and become lodged in the small blood vessels around the liver tumour where they destroy it while sparing the surrounding healthy tissue.

SIR-Spheres Y-90 resin microspheres are well tolerated and have been demonstrated to be effective in treating non-resectable, generally advanced, primary liver cancer and secondary liver metastases in patients who have failed prior chemotherapy.[2,3]

Sirtex in figures

- Sirtex supplies SIR-Spheres Y-90 resin microspheres to more than 40 countries;
- More than 1,090 treatment centres around the world use SIR-Spheres Y-90 resin microspheres;
- Over 73,000 patient treatments have been supplied.

Innovation through collaboration

Sirtex collaborated with more than 100 world-class universities and research institutions, involving more than 1,000 researchers, to innovate new approaches to help improve the life expectancy of patients with cancer.

Investigating earlier use of SIR-Spheres Y-90 resin microspheres

SIR-Spheres Y-90 resin microspheres are the most widely studied SIRT technology for treating primary and secondary liver tumours. Sirtex invested in a robust clinical trial programme of randomised clinical trials. These studies involved more than a hundred leading international medical institutions, a thousand researchers and more than 2,000 patients. They were the largest studies of their kind in the world and were designed to demonstrate the efficacy and safety of SIR-Spheres Y-90 resin microspheres as a treatment for liver tumours.

The SIRFLOX, FOXFIRE and FOXFIRE Global studies investigated the first-line use of SIR-Spheres Y-90 resin microspheres in combination with a current standard of care chemotherapy, in patients with recently diagnosed inoperable tumours in the liver that have spread from the bowel. The three studies recruited 1,103 patients to provide sufficient statistical power to examine the survival benefit from the addition of SIR-Spheres Y-90 resin microspheres to current chemotherapy. The survival data from the FOXFIRE Combined Analysis were reported at the May 2017 Annual Meeting of the American Society of Clinical Oncology (ASCO).

MEDIA BACKGROUNDER

Although SIR-Spheres Y-90 resin microspheres in combination with standard first-line mFOLFOX6 chemotherapy did not cause a superior overall survival (OS) in the studied group of patients with liver metastases from colorectal cancer, they did provide a significantly improved median OS by 4.9 months and reduced the risk of death at any given point in time by 36% when given first line in combination with standard mFOLFOX6 chemotherapy for liver-only or liver-dominant mCRC in patients with right-sided primary (RSP) tumours.[4]

The initial results of the SIRFLOX study were presented at the ASCO 2015 Annual Meeting by Professor Peter Gibbs. The final data were published on-line as a Rapid Communication in February 2016 in the *Journal of Clinical Oncology* and the paper was also included in the "*Best of JCO: 2016 Annual Meeting Edition*".[5] The editors stated that this "paper is required reading and is considered practice-changing", which suggests that the SIRFLOX regimen could potentially change the treatment journey for patients with mCRC.

The results from this first large-scale, randomised controlled trial of 530 chemotherapy-naive patients with liver-only or liver-dominant mCRC showed that there was no statistically significant improvement in PFS at any site with the addition of SIR-Spheres Y-90 resin microspheres, a finding that was not unexpected with a liver-directed treatment. However, the risk of first progression in the liver as per competing risk analysis remained significantly lower for patients receiving SIR-Spheres Y-90 resin microspheres. The improvement was 7.9 month with an HR of 0.69 corresponding to a 31% reduction in risk of progression in the liver at any point in time.

The SARAH and SIR*ve*NIB studies were two large multi-centre randomised controlled studies launched in 2010 and 2011 to compare the efficacy and safety of SIR-Spheres Y-90 resin microspheres with sorafenib in patients with intermediate or advanced hepatocellular carcinoma (HCC), respectively in Europe and in Asia. The results were presented at the European Association for the Study of the Liver (EASL) congress in April 2017 and at the ASCO 2017 Annual Meeting in June 2017, respectively.

Neither study achieved its primary endpoint of increased OS for patients treated with SIR-Spheres Y-90 resin microspheres delivered directly to liver tumours *versus* systemic oral therapy with the standard of care, sorafenib. OS did not significantly differ between the 2 groups, yet SIRT using SIR-Spheres Y-90 resin microspheres was associated with significantly fewer and less severe treatment-related adverse events than systemic treatment with sorafenib. [6,7]

A third large European study called SORAMIC is comparing treatment of HCC with SIR-Spheres Y-90 resin microspheres followed by sorafenib to treatment with sorafenib alone. Results from SORAMIC are expected to be presented at a major medical congress in 2018.

Sirtex's head office is in Australia with substantial operations in the US, Singapore and Germany.

2017 Full year financial and operating highlights

- 13 consecutive years of growth;
- Record revenues of $234.3 million, up 0.8% on the previous year;
- Record dose sales of 12,578, up 5.4% on the previous year;
- Net loss after tax of $ 26,3million;
- Cash balance of $118.3 million, up 10.6% on the previous year and no debt.

Note: All amounts are in Australian dollar.

For more information please visit:
www.sirtex.com

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4. Wasan HS *et al.* *Lancet Oncol* 2017; **18**: 1159-71
5. van Hazel GA *et al.* *J Clin Oncol* 2016; **34**: 1723–31.
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7. Chow PKH *et al.* *J Clin Oncol* 2017; **35** (Suppl): Abs 4002.