American Society of Clinical Oncology (ASCO) publishes abstract of SIR*ve*NIB, an Investigator-led Asia Pacific Primary Liver Cancer Study to be presented at ASCO Annual Meeting in Chicago, 4 June 2017

The SIR*ve*NIB abstract published on-line in the *Journal of Clinical Oncology* states that treatment of locally advanced Hepatocellular Carcinoma (HCC) with a single treatment of SIR-Spheres® Y-90 resin microspheres results in Overall Survival not significantly different from twice-daily oral sorafenib, but with significantly better tumour response and fewer and less severe adverse events

The study was conducted by The Asia-Pacific Hepatocellular Carcinoma Trials Group (AHCC) in collaboration with the National Cancer Centre Singapore and Singapore Clinical Research Institute (SCRI) and supported by the National Medical Council Singapore and Sirtex Medical Limited

Singapore (18 May 2017) – The lead author of the SIR*ve*NIB abstract, Professor Pierce Chow, Senior Consultant Surgeon at the National Cancer Centre Singapore and the Singapore General Hospital, reported that: "Asia Pacific patients with locally advanced primary liver cancer (HCC or hepatocellular carcinoma) with no spread (metastases) outside the liver who are treated with Y-90 resin microspheres have a significantly better tumour response rate (TRR) compared to sorafenib, despite 28.6% (n=52) of patients not receiving Y-90 therapy as planned (TRR - 16.5% for Y-90 resin microspheres vs 1.7% for sorafenib, respectively; $p < 0.001$). Moreover, patients experienced fewer, less serious adverse events when compared with those treated with sorafenib. There were no statistically significant differences in the primary endpoint of overall survival (OS) between the two treatments."

Although the median OS in the intent-to-treat group[1] was 8.54 months for Y-90 resin microspheres vs. 10.58 months for sorafenib, respectively (p=0.203), there was a trend in improvement in median OS in the treated group[2] for Y-90 resin microspheres (11.27

vs. 10.41 months, p=0.273). While Y-90 resin microspheres were not superior to sorafenib regarding OS, Professor Chow, who is also Professor and Course Director at the Duke-NUS Medical School, indicated that "the better tumour response and tolerability of Y-90 resin microspheres offers a compelling treatment alternative for patients with advanced hepatocellular carcinoma, for whom there are limited treatment options available."

SIR*ve*NIB was designed to compare the efficacy and safety of selective internal radiation therapy (SIRT) with yttrium-90 [Y-90] resin microspheres (SIR-Spheres; Sirtex Medical Limited, North Sydney, Australia) versus sorafenib (Nexavar®; Bayer HealthCare Pharmaceuticals, Berlin, Germany), a systemic treatment that is the current standard of care in advanced hepatocellular carcinoma. The patients in SIR*ve*NIB were ineligible for potentially curative therapies, such as surgical resection, ablation or liver transplantation.

"Each year we are making good progress in treating liver cancer. The deeper we go in our research the better we are able to understand how the cancer behaves and we are able to widen the treatments options for our patients. The results reinforced our belief that with the right people on the research project, we can get the best results. I am grateful to our partners for collaborating in this study," added Professor Soo Khee Chee, Director of NCCS.

"Completion of the investigator-led SIR*ve*NIB study represents a significant milestone in Asia Pacific liver cancer research, and underscores the strong private-public partnership that exists between Sirtex Medical Limited, the National Cancer Centre Singapore and Singapore Clinical Research Institute. We look forward to the presentation of more complete results of SIR*ve*NIB at the impending ASCO Annual Meeting," said Associate Professor Teoh Yee Leong, CEO Singapore Clinical Research Institute. "This is the first time we have completed such a large-scale investigator-led clinical trial in the Asia Pacific region, whose results will be beneficial to liver cancer patients in our region."

About Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer – cancer that starts in the liver – which is the sixth most-common cancer in the world and the second most-common cause of cancer-related death.[3] It affects mainly

patients with cirrhosis from any cause, including viral hepatitis and alcohol abuse. HCC occurs with greatest frequency in regions where hepatitis is most often diagnosed, such as in the Asia Pacific region and Southern Europe. When diagnosed in its early stages, HCC can be treated by surgical resection, ablation or liver transplantation with expectation of improved long-term survival. However, these options are not available to the great majority of patients. For patients with unresectable HCC, the outlook is bleak, with survival ranging from a few months to about two years depending largely on the extent of their tumours and state of their liver at the time of diagnosis.[4] No new HCC treatment option has been tested successfully in large studies for almost a decade.

About National Cancer Centre Singapore

National Cancer Centre Singapore (NCCS) provides a holistic and multi-disciplinary approach to cancer treatment and patient care. We treat almost 70 per cent of the public sector oncology cases, and they are benefiting from the sub-specialisation of our clinical oncologists. NCCS is also accredited by the US-based Joint Commission International for its quality patient care and safety. To deliver among the best in cancer treatment and care, our clinicians work closely with our scientists who conduct robust cutting-edge clinical and translational research programmes which are internationally recognised. NCCS strives to be a global leading cancer centre, and shares its expertise and knowledge by offering training to local and overseas medical professionals. www.nccs.com.sg

About Singapore Clinical Research Institute

Singapore Clinical Research Institute (SCRI) is a National Academic Research Organisation dedicated to enhance the standards of human clinical research. Its mission is to spearhead and develop core capabilities, infrastructure and scientific leadership for clinical research in Singapore. SCRI is a national clinical trials coordination centre that works with National Medical Research Council (NMRC) to assist the Ministry of Health in implementing clinical trials policy and strategic initiatives to support and develop clinical research competencies locally. In driving towards its vision, SCRI collaborates with clinicians to enhance Singapore's clinical research and strengthen its expertise in executing multi-site, multi-national studies

and the development of regional clinical research networks. SCRI is a wholly-owned subsidiary of MOH Holdings. http://www.scri.edu.sg

Current Availability of SIR-Spheres Y-90 resin microspheres

SIR-Spheres Y-90 resin microspheres are approved for the treatment of inoperable liver tumours in Australia, the European Union (CE Mark), Argentina (ANMAT), Brazil, and several countries in Asia, such as Turkey, India and Singapore. The product is also supplied for this use in countries such as Hong Kong, Israel, Malaysia, New Zealand, Taiwan and Thailand. SIR-Spheres Y-90 resin microspheres also have a full Pre-Market Approval (PMA) by the FDA and are indicated in the United States for the treatment of non-resectable metastatic liver tumours from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine.

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[1] Intent-to-treat group includes all patients who were enrolled and randomly allocated to treatment and are analysed according to the group to which they were randomized. The intent-to-treat-group included n=182 (Y-90 resin microspheres) and n=178 (sorafenib).

[2] Treated group includes only those patients who completed the treatment originally allocated. The treated group included n=130 (Y-90 resin microspheres) and n=162 (sorafenib).

[3] Ferlay J *et al*. Globocan 2012. v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 18/May/2017.

[4] EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol 2012; 56: 908–43.