



## **SIR-Spheres® Y-90 Resin Microspheres Showed no Significant Difference in Overall Survival (OS) Compared to Sorafenib in Advanced HCC with Significantly Fewer Severe Adverse Events, New Asia-Pacific Study Finds**

### **Final Results of SIRveNIB Study presented at 2017 American Society of Clinical Oncology Meeting**

Chicago, IL, USA (5 June 2017) -- For the second time in less than two months, a major head-to-head study has shown that SIR-Spheres Y-90 resin microspheres, administered once directly to the liver offers important treatment benefits compared to twice-daily oral doses of sorafenib, the current standard of care for advanced hepatocellular carcinoma (primary liver cancer or HCC).<sup>1</sup>

Results of the 360-patient SIRveNIB study were presented at ASCO by the Principal Investigator, Prof. Pierce Chow, Senior Consultant Surgeon at the National Cancer Centre Singapore and the Singapore General Hospital. Prof. Chow stated that, "We found that the Asian patients with locally advanced HCC who were treated with Y-90 resin microspheres had a significantly better tumour response rate of 16.5% compared to 1.7% for sorafenib ( $p < 0.001$ ) in the intent to treat, or ITT analysis, and 23.1% for SIRT compared to 1.9% ( $p < 0.001$ ) in the treated population, which represents the patients who actually received their allocated treatment. They also experienced almost a two-fold decrease in severe adverse events (grade  $\geq 3$ ; 27.7% vs. 50.6%;  $p < 0.0001$ ) compared with those treated with sorafenib."

"The primary endpoint of the study, overall survival (OS) was not met," Prof. Chow added. "If you look at patients assigned to each therapy in the ITT, analysis, median survival in the Y-90 resin microspheres study arm was 8.84 versus 10.02 months for the sorafenib group ( $p = 0.360$ ). This difference is not statistically significant. However, this analysis does not take into account that more than a quarter of the patients (28.6%; 52 patients) who were scheduled to received Y-90 therapy actually didn't receive treatment. If you look at the survival data based solely on those patients who actually received Y-90 resin microspheres, median OS was 11.3 months compared to 10.4 months for those treated with sorafenib, an opposite trend that is also not statistically significant."

"The comparative data on side effects reported in the SIRveNIB study unequivocally favoured Y-90 resin microspheres over sorafenib," Prof. Chow said. "In addition to two-fold fewer severe AEs, we observed about one fourth as many adverse events (60.0% vs. 84.6%  $p < 0.0001$ ) as well as fewer serious AEs [SAEs] (20.8% vs. 35.2%;  $p = 0.009$ ). Specifically, patients treated with Y-90 resin microspheres reported

substantially less fatigue (3.8% vs. 15.4%), diarrhoea (1.5% vs. 29.6%), hand-foot skin reaction (0.8% vs. 54.9%), alopecia (0% vs. 9.9%) as well as hypertension (0% vs. 14.8%) than those treated with sorafenib.”

Side effects specifically associated with Y-90 resin microspheres were infrequent and manageable. The incidence rate of gastric ulcer was 0.8%, upper GI haemorrhage was 1.5% (vs. 1.9% for sorafenib), jaundice was 1.5% (vs. 1.9%) and portal hypertension was 0% in the SIRT arm (vs. 0.6%), which were not significantly different from the sorafenib group. The incidence rate of radiation hepatitis (1.5%) was consistent with previously published studies.<sup>2</sup>

Although these differences were not significant in the intent-to-treat population, patients who actually received Y-90 resin microspheres in the SIRveNIB study experienced additional treatment benefits in respect to other secondary endpoints, including overall Progression-Free Survival [PFS, 6.3 vs 5.2 months, Hazard Ratio (HR) = 0.73,  $p = 0.013$ ], PFS in the liver (6.7 vs. 5.2 months, HR = 0.71,  $p = 0.09$ ), overall Time to Progression (TTP, 6.4 vs. 5.4 months, HR = 0.73,  $p = 0.019$ ) and TTP in the liver (6.8 vs 5.5 months, HR=0.72,  $p = 0.013$ ).

The findings of SIRveNIB reported at ASCO<sup>1</sup> essentially mirrored the findings of the 459-patient European SARAH study, the results of which were reported by Prof. Valerie Vilgrain, Chief of Radiology, Hôpital Beaujon, Clichy, France, at the 2017 International Liver Congress™, Amsterdam 23 April 2017.<sup>3</sup>

Tumour response rate [TRR] in SARAH was 19.0% for SIRT vs. 11.6% for sorafenib ( $p=0.042$ ).<sup>3</sup> In SIRveNIB, TRR was 16.5% vs. 1.7%;  $p<0.001$ .<sup>1</sup> Safety profiles were also quite similar. In SARAH, significantly fewer patients (76.5% vs. 94.0%;  $p<0.001$ ) treated with SIR-Spheres had any treatment-related side effects; and these were also less severe (grade  $\geq 3$ ; 40.7% vs. 63.0%;  $p<0.001$ ).<sup>3</sup> In SIRveNIB, fewer patients (60.0% vs. 84.6.0%;  $p<0.0001$ ) treated with SIR-Spheres had any side effects, severe side effects (grade  $\geq 3$ ; 27.7% vs. 50.6%;  $p<0.0001$ ) or SAEs (20.8% vs. 35.2%;  $p=0.009$ ).<sup>1</sup>

In SARAH, patients in the SIR-Spheres arm also maintained a significantly better QoL over time by Global Health Status using the EORTC QLQ-C30 questionnaire compared to those on sorafenib, who experienced a significant and sustained decline in QoL compared to baseline (group effect:  $p=0.005$ ; time effect:  $p<0.001$ ; between group difference over time:  $p=0.045$ ).<sup>3</sup>

Survival differences in neither study were significant, whether by ITT or per protocol analysis.<sup>1,3</sup> The SIRveNIB study was an investigator-initiated study 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.<sup>1</sup>

The SARAH study was an investigator study sponsored Assistance Publique – Hôpitaux de Paris (AP-HP) and supported by Sirtex Medical Limited.<sup>3</sup>

## What is Hepatocellular Carcinoma (HCC)?

HCC patients represent 90% of all people diagnosed with primary liver cancer, which is the sixth most common cancer in the world and the second leading cause of cancer-related death. HCC affects mainly patients with cirrhosis from any cause, including viral hepatitis, alcohol misuse, and fatty liver disease, and results in more than 670,000 deaths globally each year.<sup>4</sup> Among people at risk of HCC, incidence of the disease increases progressively with advancing age, reaching a peak at around 70 years.<sup>5</sup>**Error! Reference source not found.****Error! Reference source not found.****Error! Reference source not found.**

Overall, one-third of patients with liver cirrhosis will develop HCC during their lifetime.<sup>6</sup>

- Worldwide, approximately 54% of HCC cases can be attributed to HBV infection (affecting 400 million people) while 31% can be attributed to HCV infection (affecting 170 million people).<sup>5</sup>
- In Africa and East Asia, the largest attributable fraction is due to HBV infection (60%), while in the developed Western world, chronic HCV infection appears to be the major risk factor.<sup>7,8</sup>

In addition to these causes, it is now thought that up to one in eight (12.8%) of non-alcoholic steatohepatitis (NASH) patients with cirrhosis will progress to HCC.<sup>9</sup> NASH – which is widely considered to be triggered by type II diabetes, insulin resistance, obesity, hyperlipidaemia and hypertension – has become the number one cause of liver disease in Western countries. Progression of NASH dramatically increases the risks of cirrhosis, liver failure, and HCC. This is thought to be related to the worldwide epidemic of diabetes and obesity.<sup>10</sup>

HCC occurs more often in men than women, except in Africa, where more women are affected.<sup>4</sup>

## What is SIRT with SIR-Spheres Y-90 resin microspheres?

SIRT with SIR-Spheres Y-90 resin microspheres is an approved treatment for inoperable liver tumours. It is a minimally-invasive treatment that delivers high doses of high-energy beta radiation directly to the tumours. SIRT is administered to patients by interventional radiologists, who infuse millions of radioactive resin microspheres (diameter between 20–60 microns) via a catheter into the liver arteries that supply blood to the tumours. By using the tumours' blood supply, the microspheres selectively target liver tumours with a dose of radiation that is up to 40 times higher than conventional radiotherapy, while sparing healthy tissue.

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 tumours from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUDR (floxuridine).

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