

## SIRFLOX Study Abstract Released by ASCO

- SIRFLOX study shows an additional 7.9 months (20.5 months vs 12.6 months), being a 62.7% improvement, in median Progression-Free Survival in the liver for patients whose treatment included SIR-Spheres<sup>®</sup> Y-90 resin microspheres.
- Patients whose treatment included SIR-Spheres microspheres had a 31% lower risk (HR=0.69) of the tumours in their liver progressing during the time they were on the SIRFLOX study.
- Study authors confirm that median Progression-Free Survival in the liver was significantly extended and the addition of SIR-Spheres microspheres was associated with acceptable toxicity.

**Sydney, Australia; 14<sup>th</sup> May 2015** – Sirtex Medical Limited (ASX:SRX) is pleased to announce that the American Society for Clinical Oncology (ASCO) has published the SIRFLOX Study Abstract as part of the 2015 Annual Meeting Abstracts released on its website [http://abstracts.asco.org/156/AbstView\\_156\\_145884.html](http://abstracts.asco.org/156/AbstView_156_145884.html). An overview of the SIRFLOX Study Abstract is provided on the following page.

Mr Gilman Wong, CEO of Sirtex said “The reduction in the risk of tumour progression in the liver, coupled with the statistically significant nature of the result is encouraging. We look forward to the presentation of the SIRFLOX study data and associated review by the discussant and expert panel at ASCO as part of the peer review process for SIR-Spheres microspheres in first-line metastatic colorectal cancer.”

Mr Wong further commented “Sirtex’s current business continues to experience solid growth, with global dose sales up 22% in the first ten months of this financial year compared to the previous corresponding period. March and April 2015 dose sales were the two highest monthly results ever recorded.”

Following the release of the ASCO abstract, Sirtex anticipates that members of the scientific community will likely form small discussion groups to discuss the results of the SIRFLOX study data, as presented in the abstract, ahead of the ASCO meeting.

As indicated in the Sirtex ASX announcement on 21<sup>st</sup> April 2015, Associate Professor Peter Gibbs will present the findings of the SIRFLOX study data in the Gastrointestinal (colorectal) Cancer Oral Abstract Session at the ASCO Annual Meeting to be held from 3:00 p.m. to 6:00 p.m. (US Central Daylight Time) on Saturday, 30<sup>th</sup> May 2015.

Professor Ricky A. Sharma, MA, MB, BChir, FRCP, FRCR, PhD from the Gray Institute for Radiation Oncology and Biology, University of Oxford has been independently selected by the ASCO Scientific Program Committee to be the expert discussant for the SIRFLOX study results and two additional abstracts. The role of the discussant during the Oral Abstract Session is to comprehensively and critically review study data via a 12 minute themed discussion, followed by a 12 minute panel question and answer session.

Sirtex anticipates that important new information will arise from the Oral Abstract Session that facilitates a greater understanding of the implications and impact of the SIRFLOX study for SIR-Spheres® Y-90 resin microspheres in first-line mCRC, and how this may apply to clinical practice.

Sirtex will host an investor conference call following the presentation at ASCO by Associate Professor Peter Gibbs, with details to follow.

### Overview of SIRFLOX Study Abstract

The SIRFLOX study results revealed a statistically significant improvement in median Progression-Free Survival (PFS) in the liver. Reported median PFS in the liver was 20.5 months in the SIR-Spheres microspheres + mFOLFOX6 chemotherapy ± biologic agent bevacizumab (bev) arm versus 12.6 months in the mFOLFOX6 ± bev arm, with a P value  $p=0.002$  and a Hazard Ratio of  $HR=0.69$ . This means that there was less than a 0.2% chance the result in the liver was due to chance alone and that there was a 31% reduction in the risk of tumour progression in the liver for patients whose treatment included SIR-Spheres microspheres while on study.

A summary of the other key findings in the SIRFLOX Study Abstract were:

- Overall Progression-Free Survival (PFS), the primary endpoint of the SIRFLOX study was not improved in a statistically significant way via the addition of SIR-Spheres microspheres. Median overall PFS was 10.7 months in the SIR-Spheres microspheres + mFOLFOX6 ± bev arm versus 10.2 months in the mFOLFOX6 ± bev arm, with a P value  $p=0.428$  and a Hazard Ratio of  $HR=0.93$ .
- Overall Tumour Response Rate (RR), a secondary endpoint in the SIRFLOX study was 76.4% in the SIR-Spheres microspheres + mFOLFOX6 ± bev arm versus 68.0% in the mFOLFOX6 ± bev arm, with a P value of  $p=0.113$ .
- Hepatic Response Rate, a secondary endpoint in the SIRFLOX study was 78.7% in the SIR-Spheres microspheres + mFOLFOX6 ± bev arm versus 68.8% in the mFOLFOX6 ± bev arm, with a P value of  $p=0.042$ .
- The Complete Response Rate in the liver was 6.0% in the SIR-Spheres microspheres + mFOLFOX6 ± bev arm versus 1.9% in the mFOLFOX6 ± bev arm, with a P value of  $p=0.02$ . This result indicates that patients who received SIR-Spheres microspheres as part of their treatment experienced approximately a threefold higher rate of complete disappearance of tumours in their liver, compared to patients who did not receive SIR-Spheres microspheres.
- Liver Resection Rate, a secondary endpoint in the SIRFLOX study was 14.2% in the SIR-Spheres microspheres + mFOLFOX6 ± bev arm versus 13.7% in the mFOLFOX6 ± bev arm, with a P value of  $p=0.857$ .
- The Overall Survival (OS) data from the SIRFLOX study is required to be combined with the FOXFIRE and FOXFIRE Global studies to provide sufficient statistical power in over 1,000 patients globally to detect a clinical significant difference in OS between the SIR-Spheres microspheres and control arms. Analysis of OS from the SIRFLOX study cannot be progressed at this time for reasons of (a) bias and (b) statistical power for these studies. Overall OS data is anticipated during 1H CY17.

The study authors concluded “In first-line treatment of pts with non-resectable CRC liver metastases, the addition of SIRT to standard chemotherapy failed to improve overall PFS. However, median liver PFS was significantly extended. The addition of SIRT was associated with acceptable toxicity. Overall survival analyses, combining data from SIRFLOX and two other ongoing studies in this disease setting, are awaited.”

*A Glossary of key clinical study and statistical terminology used in this release is included at the end of the announcement. Further details of certain terminology can be found in the 'Expert Clinician Presentation to Investors' ASX release on 10<sup>th</sup> December 2014*

## **About ASCO**

The ASCO Annual Meeting brings together 30,000 oncology professionals from around the world. Educational sessions feature world-renowned faculty discussing state-of-the-art treatment modalities, new therapies, and ongoing controversies in the field. Science sessions present the latest ground-breaking research in oral and poster format. Sirtex will have an exhibit booth (#10135) at the ASCO Annual Meeting from 29<sup>th</sup> May to 2<sup>nd</sup> June.

## **About SIRFLOX**

The SIRFLOX study is an international, multi-centre, randomised controlled study that enrolled over 500 patients with mCRC whose disease was non-resectable and had spread to either the liver alone or the liver plus a limited number of sites outside the liver, including lymph nodes and the lungs. The study was conducted in more than 100 hospitals across Australia, Europe, Israel, New Zealand and the United States. SIRFLOX is the first, large randomised controlled study that has examined the use of Selective Internal Radiation Therapy (SIRT, also known as radioembolisation) in the treatment of colorectal liver metastases. For more information, please visit [www.sirflox.com](http://www.sirflox.com) and the ASX announcement made by Sirtex on 9<sup>th</sup> October 2014.

## **About SIR-Spheres<sup>®</sup> Y-90 Resin Microspheres**

SIR-Spheres Y-90 resin microspheres are a medical device used in interventional oncology to deliver Selective Internal Radiation Therapy or SIRT (also known as radioembolisation), a proven technology for inoperable liver tumours that delivers substantial, targeted doses of radiation directly to the cancer. Key SIR-Spheres Y-90 resin microspheres regulatory approvals include Pre-Market Approval (PMA) from the US FDA, European Union (CE Mark) approval and Australian TGA approval.

## **About Sirtex Medical**

Sirtex Medical Limited (ASX:SRX) is an Australian-based global healthcare business working to improve outcomes in people with cancer. Our current lead product is a targeted radiation therapy for liver cancer called SIR-Spheres<sup>®</sup> 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 [www.sirtex.com](http://www.sirtex.com).

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## GLOSSARY OF TERMS

*Primary Endpoint* – the main treatment outcome that is measured to compare the effectiveness of the investigational treatment to the control (reference) treatment. In the SIRFLOX study the primary endpoint was Progression-Free Survival.

*Secondary Endpoint* – additional treatment outcomes that are measured to enable comparisons of the effectiveness, safety, tolerability, cost etc. of the investigational treatment to the control (reference) treatment. In the SIRFLOX study the secondary endpoints were Progression-Free Survival in the Liver, Overall Survival, Tumour Response Rate, Tumour Recurrence Rate, Quality-of-Life, Toxicity and Safety, and Liver Resection Rate.

*Progression-Free Survival (PFS)* – the time elapsed from the date of patient randomisation until the date of tumour progression occurring at *any site in the body* (or patient death if disease progression has not yet occurred). In plain language, PFS measures the duration of time that tumours located at any site in the body are ‘not growing’.

*Overall Progression-Free Survival (PFS)* – synonymous with Progression-Free Survival, above.

*Progression-Free Survival (PFS) in the Liver* – the time elapsed from the date of patient randomisation until the date of tumour progression occurring *in the liver* (or patient death if disease progression in the liver has not yet occurred). In plain language, PFS in the Liver measures the duration of time that tumours located in the liver are ‘not growing’.

*Overall Survival (OS)* – the time elapsed from the date of patient randomisation until the date of patient death. In plain language, OS measures the duration of time that the patient remains ‘alive’.

*Tumour Response Rate (RR)* – the percentage of patients experiencing either a Complete Response or Partial Response, based on assessment of *all of the tumours* present in the body. In plain language, RR measures the percentage of patients experiencing either complete or partial ‘shrinkage’ of their tumours located at any site in the body.

*Overall Tumour Response Rate (RR)* – synonymous with Tumour Response Rate, above.

*Hepatic Response Rate* – the percentage of patients experiencing either a Complete Response or Partial Response, based on assessment of *tumours in the liver*. In plain language, Hepatic RR measures the percentage of patients experiencing either complete or partial ‘shrinkage’ of their tumours located in the liver.

*Complete Response (CR)* – disappearance of all target lesions associated with the disappearance of all non-target lesions. In plain language, CR means complete ‘disappearance’ of all tumours.

*Partial Response (PR)* – at least a 30% decrease in the sum of the longest diameter of the target lesions, taking as reference the baseline sum longest diameters. In plain language, PR means at least 30% ‘shrinkage’ of all tumours.

*Liver Resection Rate* – the percentage of patients undergoing surgical removal of the tumours in their liver.

*Hazard Ratio (HR)* – defines the relative risk of the event (e.g. tumour progression if the primary endpoint of the study is PFS, or death if the primary endpoint of the study is OS) occurring in the investigational arm compared to the control arm. For example, if the primary endpoint of the study is Overall Survival, a HR of 0.75 means that a patient receiving the investigational treatment has a 25% lower risk of death during the study compared to a patient receiving the control treatment; a HR of 1.0 means that a patient has the same risk of death during the study between the investigational treatment and the control.

*P Value* – defines how likely the study result was due to chance alone rather than the effect of the treatment. By convention, if the P Value is less than 0.05 ( $p < 0.05$ ) the results are deemed statistically significant. For example, if  $p = 0.001$  there was a 1 in 1,000 chance that the study result was due to chance alone and not due to the effect of treatment.