ASX Announcement

1 May 2024

1st Study in Man Shows Therapy Increases Pancreatic Tumor Vascularity Adding OncoSil™ to Chemotherapy Significantly Increased the Vascularity of Pancreatic Cancer Primary Tumors

Key Highlights

- ✓ **First study in humans demonstrating that the vascularity of pancreatic cancer primary tumors can be increased;**
- ✓ **The study assessed changes to the vascularity of primary pancreatic cancer tumors by chemotherapy and following the implantation of OncoSil™ in tumors in patients with locally advanced pancreatic cancer;**
- ✓ **The addition of OncoSil™ resulted in a substantial increase in tumor vascularity, along with a significant decrease in tumor size;**
- ✓ **Historical controls show no increase in vascularity from chemotherapy alone;**
- ✓ **In addition to delivering a tumorcidal dose of radiotherapy to the pancreatic tumor, OncoSil™ increases tumor vascularity and it is believed therefore the concentration of chemotherapy within the tumor.**

Christchurch, New Zealand, 1 May 2024: Pancreatic cancer treatment device company **OncoSil Medical Limited (ASX: OSL)** (**OncoSil** or the **Company**) is pleased to announce the results of a study showing that the addition of OncoSil™ to systemic chemotherapy significantly increases the vascularity of the primary pancreatic tumors and at the same time results in a significant decrease in the size of the tumours.[1] This is believed to be the first study in humans demonstrating that the poor vascularity of pancreatic cancer tumors can be increased, which may consequently increase the concentration of chemotherapy agents within the tumor and further explains the mode of action of OncoSil™.

The prospective, investigator-initiated study recruited patients with unresectable, non-metastatic locally advanced pancreatic cancer (LAPC) undergoing standard FOLFIRINOX chemotherapy plus OncoSil™ implantation after 2 or 3 cycles of chemotherapy. Patients were assessed using contrast-enhanced harmonic EUS (CH-EUS) after 2 cycles of chemotherapy and at 4 weeks and 12 weeks after OncoSil™ implantation, in addition to the evaluation of tumor response by CT imaging.

Twenty patients were recruited, with 15 completing 12-week follow-up. After 2 cycles of chemotherapy and prior to OncoSil™ implantation, all tumors demonstrated a lower intensity of enhancement relative to surrounding normal pancreatic tissue, suggesting low vascularity (hypovascularity) with a median intensity gain of 32.15 (IQR 18.08–54.35) by CH-EUS. The median intensity gain increased to 46.85 (IQR 35.05–76.6; p=0.007) and 66.3 (IQR 54.7–76.3; p=0.001) at 4 weeks and 12 weeks after OncoSil™ implantation, respectively, indicating that vascularity increased significantly in the treated tumors. Historical data showed no changes in vascularity in response to treatment using chemotherapy alone.

In parallel, the longest diameter of the primary tumors decreased from a median of 32mm (IQR 27.5–38.75) pre-implantation to 24mm (IQR 16–26) 12 weeks post-implantation ($p<0.001$), demonstrating a significant response to treatment using OncoSil™ added to FOLFIRINOX chemotherapy.

At 12 weeks following OncoSil™ implantation, the local disease control rate was 100%. To date, 5 patients (25%) had their tumors downstaged, with 3 patients undergoing surgical resection to remove the primary tumor, another patient with surgery pending and one patient having refused surgical treatment. The investigators noted that this was the first clinical study to demonstrate increased vascularity within pancreatic primary tumors.

The study was conducted at the Royal Adelaide Hospital, South Australia. The results were presented by Dr Amanda Lim, from the Royal Adelaide Hospital at the 54th Annual Scientific Meeting of the Australian and New Zealand Society of Nuclear Medicine (ANZSNM) in Christchurch, New Zealand, 26–28 April 2024.

The prognosis of pancreatic cancer has not improved substantially over the last four decades, with patients facing a 5-year survival rate of 10% or less. One of the key problems is that the primary pancreatic cancer tumor is resistant to treatment due to the dense stroma (fibrotic tissue) surrounding it, an immunosuppressive environment and poor vascularity that limits the concentration of chemotherapy reaching the tumor. In addition, the dose of external beam radiotherapy that can be given to pancreatic tumors is limited to 56 Gy due to the sensitivity of surrounding organs such as the stomach, bowel, kidneys, and spine. In contrast, intra-tumoural implantation of OncoSil™ delivers 100 Gy to the target tumor, with a negligible amount of radiation reaching the surrounding tissues.

OncoSil's CEO and Managing Director, Mr Nigel Lange said:

"This is an important study that further explains the mode of action of OncoSil™. In addition to delivering a tumorcidal dose of radiation therapy inside the primary pancreatic tumor that leads to significant tumor shrinkage and prolonged local disease control, this study demonstrates that the OncoSil™ device substantially increases vascularity within the tumor, which may in turn increase the concentration of chemotherapy agents that are widely acknowledged as otherwise being sub-optimal in this devastating disease."

References

1. Lim AH, Zobel J, Bills M et al. The impact of combined chemotherapy and intra-tumoral injection of Phosphorus-32 microparticles on vascularity in locally advanced pancreatic carcinoma. Presented at the 54th Annual Scientific Meeting of the Australian and New Zealand Society of Nuclear Medicine (ANZSNM) in Christchurch, New Zealand.

Authorisation & Additional Information

This announcement was authorised by the Chairman of OncoSil Medical Limited.

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About OncoSil Medical

OncoSil Medical Limited (ASX:OSL) has developed a cancer treatment device, the OncoSil™ brachytherapy device, which is a critical component of a revolutionary brachytherapy treatment for locally advanced unresectable pancreatic cancer. This type of cancer is the 12th most common cancer in men and the 11th most common cancer in women across the globe, with some 500,000 new cases of pancreatic cancer detected every year. With pancreatic cancer typically diagnosed at a later stage, it has a poor prognosis for long-term survival[1].

The OncoSil™ device delivers a targeted intratumoural placement of Phosphorous-32 (^{32}P) in the treatment of locally advanced unresectable pancreatic cancer. This occurs via injection directly into a patient's pancreatic tumours under endoscopic ultrasound guidance and takes place in combination with gemcitabine-based chemotherapy.

The OncoSil™ device that has already received breakthrough device designation in the European Union, United Kingdom and United States for the treatment of locally advanced unresectable pancreatic cancer in combination with chemotherapy. CE Marking has additionally been granted for the OncoSil™ device, which can be marketed in the European Union, United Kingdom.

While clinical trials involving the OncoSil™ device continue to occur, the Company is simultaneously moving to commercialise this unique medical technology. It is currently approved for sale in 30+ countries including European Union, United Kingdom, Türkiye and Israel, with initial commercial pancreatic cancer treatments using the device already undertaken in Spain, Italy and Israel.

To learn more, please visit: www.oncosil.com/

References: 1. https://www.wcrf.org/cancer-trends/pancreatic-cancer-statistics/