MEDICAL AND SCIENTIFIC COMMITTEE

ANNUAL LAY REPORT 2015

Lay Project Title:	A collaboration to drive clinically meaningful research into mesothelioma
Chief Investigator(s):	Dr Thomas John, A/Prof Paul Mitchell, Dr Vinod Ganju, Prof Jonathan Cebon, Mr Simon Knight
Unit/Institution:	Medical Oncology, Olivia Newton-John Cancer and Wellness Centre
Years Funded:	2014-2016

1 Lay Abstract

The initial year of the project was designed to set up a resource that could be used for clinically meaningful research. This has been achieved with a tissue microarray (TMA), clinical annotation and data correlating clinical endpoints showing that the data from the TMA is similar to that published by other groups. The significant factor is that the number of patients on the TMA is double that from other published groups, making the results more clinically important. The TMA itself is a glass slide used in microscopy on which we are able to put tissues for up to 30 different patients in triplicate. This allows us to perform stains for multiple markers rapidly and with reduced expense.

Using the patients and the TMA, we have looked at the immune infiltrate in mesothelioma and specifically investigated a marker called PD-L1 that has been reported to predict benefit from a class of immunotherapeutics called immune check-point inhibitors. We found that PD-L1 was expressed in around 25% of cases, but that its expression was associated with poorer overall survival. These data suggest that if the immune therapies work in patients whose tumours have this marker, it may also improve survival. However further research is required towards this. We also found that tumours that were positive for PD-L1 were also more likely to have a strong infiltrate of immune cells. Also suggesting that the immune system is primed to act, but is being inhibited by tumour cells evading immunological killing by increasing PD-L1 on their cell surface.

Building on this work, we have also asked whether there are genetic changes that may correlate this immune infiltrate and PD-L1 expression. In lung cancer, having a large number of mutations within the tumour appears to correlate with response to immune checkpoint inhibitors. We used a platform called Oncoscan on 66 cases to determine whether the percentage of genetic abnormalities may also correlate with PD-L1 expression. This technology enables us to look for parts of genes that are missing or mutated. Interestingly in mesothelioma we found the opposite to that reported in lung cancer. That most of the tumours with a large percentage of their genomes altered were in fact negative for PD-L1. We want to expand this observation and are currently looking to send a further 48 samples for Oncoscan in order to validate our initial findings.

2 Please list <u>all papers arising from this research project</u>, which have been published, or accepted for publication, in refereed journals since the commencement of this grant. Please list in chronological order, include title, sequence of authors, first, and last pages, name, volume and date of journal.

Briefly annotate major findings within these publications

	We have several papers that are close to publication. The main body of work is waiting for the Oncoscan data on the further 48 samples. There are two invited review papers that are due end of February that we have been working on. The first is on immunological treatments in mesothelioma and the second on the tumour microenvironment in mesothelioma. There is a paper looking at a marker called Caveolin and Calretinin that we are reviewing the final drafts prior to submission. This substudy was suggested by the pathologist we were able to retain for the project. He had read and was keen to use Caveolin as a mesothelioma marker in order to differentiate the histological subtypes of mesothelioma. However although Caveolin was a useful marker it did not correlate with the sarcomatoid histology as first thought.
3	**Please list any presentations relating to this research project that were made at scientific meetings during 2015.** *Please identify the meeting, provide the tile of your presentation and indicate the type of presentation (plenary, invited, selected, poster etc, or session chair)* Chair: ASCO 2015 Lung Cancer and Mesothelioma mini-oral session Invited Speaker: International Conference on Asbestos
4	**Certification by Chief Investigator**
	I confirm that the above details are correct. Signature: _  _____Date: 16th Feb 2016 Thomas John