RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Melanoma Immunotherapy and Positron Emission Tomography
Name	Dr Annie N. M. Wong
Award Received	2016 Vincent Fairfax Postgraduate Research Entry Scholarship
Report Date	27 March 2017
Chief Investigator / Supervisor	Professor Grant McArthur
Administering Institution	The University of Melbourne
Funding Period Start Date:	1 January 2016
Finish Date:	31 December 2016

PROJECT SUMMARY

Melanoma immunotherapy has dramatically improved the survival and quality of life for patients with advanced melanoma. However, not all patients respond to these treatments, and it can potentially cause severe side effects. These medicines are also extremely expensive. Therefore, it is important to find ways to identify those who are likely to respond, and also to stop futile treatment as soon as possible.

This project aims to use functional positron emission tomography (PET) scans to identify patients who are likely to respond to these immunotherapies and also explore how these functional scans can be used to assess whether the treatments are working.

PROJECT AIMS / OBJECTIVES

Aims:

1) To correlate baseline and on-treatment PET parameters with survival and toxicity outcomes for patients treated with ipilimumab and anti-PD1 monoclonal antibody for metastatic melanoma

2) To identify the relationship between baseline PET parameters together with molecular and cellular markers of the tumour microenvironment for patients treated with ipilimumab and anti-PD1 monoclonal antibody for metastatic melanoma.

3) To interrogate the mechanism of immune flare response induced by immunotherapy treatment using preclinical models

4) To assess ulceration as a predictive biomarker (in addition to its known prognostic property)

5) Explore the clinical utility of biomarkers in therapeutic decision making

SIGNIFICANCE AND OUTCOMES

The novel functional positron emission tomography parameter of high spleen to liver ratio was identified to be correlated with poor survival after immunotherapy (anti-CTLA4 and anti-PD1) for advanced melanoma. Results were presented at American Society of Clinical Oncology annual scientific meeting 2016, and was awarded a Merit Award for this poster abstract

Clinical data of patients with advanced melanoma who were treated with immunotherapy at Peter MacCallum Cancer Centre has contributed to a number of retrospective studies assessing efficacy

and toxicity in special patient cohorts, including:

- Patients with rheumatoid arthritis treated with anti-CTLA4
- Patients with underlying auto-immune conditions treated with anti-PD1
- Patients with brain metastases treated with anti-PD1
- Patients with poor performance status treated with anti-PD1

PUBLICATIONS / PRESENTATIONS

Publications

2017: Clinical and palliative care outcomes for patients of poor performance status treated with anti-programmed death 1 monoclonal antibodies for advanced melanoma

A.N.M. Wong, M. Williams, D. Milne, K. Morris, P. Lau, O. Spruyt, S. Fullerton and G.A. McArthur .

Accepted for publication in Asia Pacific journal of Clinical Oncology 2017

2017: The Advantages and Challenges of Using FDG PET/CT for Response Assessment In Melanoma In the Era of Targeted Agents and immunotherapy

A.N.M. Wong, M. Hoffman, Rod Hicks and Grant McArthur

Accepted for publication in European journal of Nuclear Medicine and

Molecular Imaging 2017

2016: Anti-PD1 therapy in patients with advanced melanoma and pre-existing autoimmune disorders or major toxicity with lpillmumab

A. M. Menzies, D. B. Johnson, S. Ramanujam, V. G. Atkinson, A. N. M. Wong,).]. Park,). L McQuade, A N. Shoushtari, K. K. Tsai, Z. Eroglu, 0. Klein,]. C. Hassel,]. A. Sosman, A. Guminski, R.]. Sullivan, A Ribas, M. S. Carlino, M.A. Davies, S. K. Sandhu, G. V. Long

Ann Oncol (2017) 28 (2): 368-376.

DOI:https://dol.org/10.1093/annonc/mdw443

2016: Integration of lmmuno-Oncology and Palliative Care

A Wong, S Fullerton, 0 Spruyt, B Brady, G McArthur and S Sandhu

Journal of Clinical Oncology. 2016 Feb 29 do/:10.1.200/JC0.2015.64.4146

2016: The use of ipilimumab in patients with rheumatoid arthritis and metastatic melanoma

Blee, A Wong, D Kee, P Neeson, M Shackleton, G McArthur and S Sandhu

Annals of Oncology. 2016 Feb 9. doi: 10.1093/annonc/mdWOS6

Presentations

2016: Spleen to liver ratio (SLR): Novel PET imaging biomarker for prediction of overall survival after ipilimumab and anti-PD1 in patients with metastatic melanoma.

Wong A, Callahan J, Beresford], Herschtal A, Fullerton S, Milne D, Hicks R, McArthur G

Poster of American Society of Clinical Oncology ASM 2016

2016: Anti-PD1 therapy in patients with advanced melanoma and persisting autoimmune disorders (AD) or major toxicity with ipilimumab (IPI)

Menzies A, Johnson D, Ramanujom S, Aktinson V, Wong A, Park}, McQuade J, Shoushtarl A, Tsai K, Eroglu z Klein 0, Hassell J, Sosman J, Guminski A, Sullivan R, Ribas A, Carlino M, Davies M, Sandhu S, Long G.

American Society of Oncology ASM (Poster discussion)

2016: Performance status as a predictor of response to anti-PD1 for metastatic melanoma

A.N.M. Wong, M. Williams, D. Milne, K. Morris, P. Lau, 0. Spruyt, S. Fullerton and G.A. McArthur

Poster at Medical Oncology Group of Australia ASM

2016: Efficacy of anti-PD1 therapy in patients with melanoma brain metastases

J Park, S Parakh, S Mendis, R Roi, W Xu, S Lo, M Drummond, C Rowe7, A Wong, G McArthur, A Haydon, M Andrews,] Cebon, A Guminski, R Ke/ford, G long, A Menzies, 0 Klein and M Carlino

Poster presented at the European Society of Medical Oncology ASM 2016

2016: Spleen to liver ratio (SLR): Novel PET Imaging biomarker for prediction of overall survival after ipilimumab and anti-PD1 in patients with metastatic melanoma.

A Wong,} Callahan,] Beresford, A Herschtal, S Fullerton, D Milne, R Hicks, G McArthur

Poster at American Society of Clinical Oncology ASM 2016 (awarded Merit Award)

2016: Anti-PD1 therapy in patients with advanced melanoma and persisting autoimmune disorders (AD) or major toxicity with ipilimumab (IPI)

A Menzies, D Johnson, S Ramanujam, V Aktinson, A Wong,] Park, J McQuade, A Shoushtari, K Tsai, Z Eroglu, 0 Klein,] Hassel,] Sosman, A Guminski, R Sullivan, A Ribas, M Carlino, M Davies, S Sandhu, G Long

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J Park, S Parakh, S Mendis, R Roi, W Xu, S lo, M Drummond, C Rowe7, A Wong, G McArthur, A Haydon, M Andrews,} Cebon, A Guminskf, R Kelford, G Long, A Menzies, 0 Klein and M Carlino

Poster presented at the European Society of Medical Oncology ASM 2016

American Society of Clinical Oncology Merit Award 2016, awarded for poster abstract, 'Spleen to liver ratio (SLR): Novel PET imaging biomarker for prediction of overall survival after ipilimumab and anti-PD1 in patients with metastatic melanoma.'