

ESMO Research Research Fellowship
(October 2021 – October 2022)

Dr John Greene

FINAL REPORT

Host Institute: University of Oxford, Oxford, OX3 7LE, United Kingdom

Mentor: Dr Simon Lord

Project title: The impact of obesity on survival outcomes following drug treatment for advanced malignancy recorded within the Systemic Anti-Cancer Therapy (SACT) database

Home Institute: St. James's Hospital, Dublin 8, Ireland

Introduction

Obesity has been linked to poorer prognosis in cancer patients, however observational data conversely suggests that some obese patients with cancer may have a better prognosis. The Systemic Anti-Cancer Therapy (SACT) database collects data for systemic anti-cancer therapy activity across all NHS hospitals in England

Rationale and Aim

The rationale and aim of this project was to test the hypothesis that obesity in a 'real world population' is linked to variable outcomes in different tumour types for patients undergoing therapy for advanced cancer. The study's aim was to map the prevalence of obesity in UK cancer patients and describe how body mass index (BMI) changes over the cancer patient journey. The contribution of obesity to patient survival and other variables would be assessed for the whole cohort, and different tumour types and therapy classes.

Experimental design

The Systemic Anti-Cancer Therapy (SACT) database collects data on chemotherapy regimens, drugs, treatment intent, performance status, height and weight across all NHS hospitals in England.

The association between BMI (high BMI: ≥ 25 kg/m² v low BMI: < 25 kg/m²) on survival following treatment with targeted therapy and immunotherapy was investigated using databases provided from the SACT database provided in Excel format. Databases contained information including cancer type, treatment, performance status and survival. Using R programme statistical software, survival from commencement of therapy with targeted anti-VEGF therapy (sunitinib, pazopanib, axitinib, cabozantinib, tivozanib), MTOR inhibitor (everolimus, temsirolimus) or immunotherapy (ipilimumab, nivolumab) was estimated by the life-table method. Mortality rate ratios were estimated by Poisson regression and adjusted by year of diagnosis, age, sex, tumour grade, performance status, Charlson score, prior nephrectomy and systemic therapy. Patients were excluded from the analysis if data on height or weight was incomplete or if enrolled on a clinical trial.

Results, Conclusions and Future Perspectives

I was able to work with a statistician at the Dept of Population Health, University of Oxford, Dr Zhe Wang who demonstrated to me how to clean large data sets in order to perform statistical analysis. By cleaning and focusing on kidney cancer, I was able to focus on a select group of patients and investigate the impact of obesity on these patients.

A total of 1,228 patients with advanced RCC receiving treatment between 2010 and 2018 were included in the analysis. The majority of patients were male (72% vs 28%), had a performance status of 0 to 1 (87%) and a Charlson co-morbidity score of 0 (84%). The majority of patients received treatment with targeted anti-VEGF therapy (84.2%). 470 patients (38.3%) had undergone cytoreductive nephrectomy, the majority of which occurred in high BMI patients (70%, $p = 0.01$). Median overall survival for patients with BMI < 25 kg/m² was 11.8 months (95% CI; 10.2-14.2) versus 19.2 months (17.2-20.7) for patients with BMI ≥ 25 kg/m² ($p < 0.001$). Therefore, high BMI is associated with improved survival in patients with metastatic RCC who have been predominantly treated with targeted anti-VEGF therapy. Improved survival in obese patients may be associated with less aggressive disease or a better response to systemic therapies and further studies of the impact of BMI on outcomes are needed, particularly in the era of immunotherapy.

Results to date demonstrate an improved survival in patients with metastatic renal cell cancer with higher BMI compared to patients with normal or low BMI. Further analysis will investigate if lower BMI negatively impacts outcome compared to those with normal or higher BMI. Further analysis

could be performed in other cancers to further examine the impact of BMI on outcomes.

List of Publications and Presentations Resulting from the Research Project:

Draft manuscript written, for submission to Cancer Control Journal:

The impact of body mass index on clinical outcomes for patients receiving systemic anti-cancer therapies for advanced renal cell carcinoma

Authors:

John Greene, Zhe Wang, Benjamin Harris, David Dodwell, Simon Lord

EMUC22

Status: Accepted

Last updated: 29 September 2022, 10:16

The impact of body mass index on clinical outcomes for patients receiving systemic anti-cancer therapies for advanced renal cell carcinoma

Topic: 13-F.6: Renal Tumour - Follow up, Clinical / Prognosis

Presentation type: EMUC Poster

List of Publications and Presentations resulting from other projects during the fellowship period (if applicable)

During my fellowship in Oxford, I had the opportunity to write a review paper with my mentor Dr Simon Lord on early phase drug development with a focus on targeting oxidative phosphorylation. This review was published in Seminars in Cancer Biology Journal.

Targeting OXPHOS and the electron transport chain in cancer; Molecular and therapeutic implications. Greene J, Segaran A, Lord S.

Semin Cancer Biol. 2022 Feb 2;S1044-579. PMID: 35122973



Selection of Courses and Workshops Attended During the Fellowship

ESMO Annual Congress, Paris September 2022.

Acknowledgements

I would like to acknowledge the support and mentoring from Dr Simon Lord, Dr David Dodwell and the invaluable statistical support provided by Dr Zhe Wang.

Personal Statement

The ESMO Fellowship provided me the opportunity to work and collaborate at the University of Oxford, a world class institution and leader in cancer research and drug development. I was able to participate in the early phase clinical trials unit under the mentorship of Dr Simon and gain invaluable experience in early phase clinical trials. I also had the opportunity to develop and improve my skills as a researcher at the Department of Population Health, University of Oxford under Dr David Dodwell. I was able to develop my skills in analysing complex cancer data, performing statistical analysis, interpreting this data and presenting it in a logical method.

I have developed relationships with colleagues that I will use when developing my own research career back in Ireland.

The supportive and collegial atmosphere at Oxford has helped me gain confidence in my own skills as a researcher and I look forward to using these skills and developing collaborative relationships in the future with my colleagues in Oxford.

I would recommend an ESMO fellowship at Oxford to any researcher pursuing a career in research and drug development.

This ESMO Clinical Research Fellowship Research Project was supported by an educational grant from ESMO.