



**Abstract 776 Figure 4**

The percentage of circulating CD3+PD-1+ cells and CD3+CD4+TIGIT+ cells positively correlated with a better treatment response in the post-treatment setting. The percentage of CD3+, CD3+CD4+ and CD3+CD8+ cells expressing ICs in peripheral circulation and infiltrating OAC tissue in the post-neoadjuvant treatment setting was correlated with each other, patient demographics and clinical features of the tumour. Patient demographics and clinical features included gender (female=0, male=1), age, tumour type (OAC=0 and OGJ=1), neo-adjuvant treatment received (CROSS=0 and FLOT=1), treatment response (determined by radiographic features using PET/CT), tumour regression grade (TRG), clinical tumour stage and nodal involvement, pathological tumour stage and nodal involvement, body mass index (BMI kg/m<sup>2</sup>), peri-neural invasion, serosal invasion and lymph-vascular invasion. BMI and weight measurement was recorded post-treatment. Spearman correlation. Only significant data shown.

as a result of an induced-anti-tumour immune response following immunogenic chemotherapy/chemoradiotherapy treatment and may be a useful strategy for stratifying patients into chemotherapy/chemoradiotherapy responders or non-responders. A therapeutic rationale is also highlighted for combining ICIs with chemotherapy regimens in OAC patients to enhance anti-tumour T cell-mediated responses and potentially boost response rates to chemotherapy treatment.

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**Ethics Approval** The work was performed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human samples.

**Consent** Patients provided informed consent for sample and data acquisition, and the study received full ethical approval from the St. James's Hospital/AMNCH Ethical Review Board.

#### REFERENCES

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#### PRECLINICAL STUDY USING A GLUTAMATERGIC SIGNALING AND IMMUNE-CHECKPOINT INHIBITORS IN A SPONTANEOUS MELANOMA PRONE MOUSE MODEL

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**Background** Much progress has been made in understanding melanoma pathogenesis within the last few years through targeted therapies and immunotherapies. However, resistance to small molecule inhibitors remains an obstacle. Immunotherapies such as checkpoint inhibitors against PD-1/PD-L1 lead to durable responses but only in a subset of melanoma patients. Mouse models reflecting human cancers provide invaluable tools towards the translation of basic science discoveries to clinical therapies, but many of these in vivo studies are short-term and do not accurately mimic patient circumstances. Our lab has a melanoma-prone transgenic mouse model which is driven by ectopic expression of a normal neuronal receptor, metabotropic glutamate receptor 1 (GRM1). This mouse model recapitulates melanoma development and progression frequently associated with melanoma patients, where aberrant GRM1 expression is detected. We have shown that in >90% of late-stage melanoma patients, there is atypical GRM1 mediated signaling and expression.

**Methods** In this study, we are using these mice, TGS, to determine the long-term, 18-week, therapeutic consequences of troriluzole, a prodrug for riluzole, which is an inhibitor of glutamatergic signaling plus anti-PD-1, an immune-checkpoint inhibitor. Tumor burden is monitored every 6 weeks for 18 weeks using a small imaging system, IVIS and tumor burden is quantified using ImageJ software. Blood, lymphoid, and tumor samples were collected at several time points during the study for molecular, and immune analyses.

**Results** Preliminary results suggest a gender-biased treatment response and that the combination of troriluzole and anti-PD-1 is more efficacious than either agent alone. In males, a 43.9% reduction in tumor burden was observed while in females there was a 29.6% increase in tumor burden in the combination group compared to vehicle. In concordance, after the removal of the treatment modality, the male mice in the combinatorial group survived 42 days longer compared to vehicle controls with sustained tumor reduction by 68.3%. In female mice no significant advantage in survival or reduction in tumor burden was noted.

**Conclusions** N/A

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#### IMMUNE CHECKPOINT BLOCKADE IMPACTS THE SUPPRESSIVE PHENOTYPE AND FUNCTION OF REGULATORY T CELLS IN AN ENDOGENOUS MOUSE LYMPHOMA MODEL

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**Background** Antibodies against programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) have become established part of anti-cancer therapy.