

AB107. SOH21AS190. Timing is everything; manipulating the surgery induced immunosuppressive milieu into a therapeutic target

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Background: Immune checkpoint inhibitors (ICIs) are being investigated for their role as an adjunct in the multimodal treatment of oesophageal cancer. The most appropriate time to incorporate ICIs remains unknown. Our study profiles systemic anti-tumour immunity perioperatively to help inform the optimal timing of ICIs into current standards of care for oesophageal adenocarcinoma (OAC) patients.

Methods: Systemic immunity was immunophenotyped pre- and post-oesophagectomy on days 0, 1, 3, 7 and week 6 by flow cytometry (n=14). The frequency of circulating lymphocytes, T cells, cytotoxic and helper T lymphocytes was profiled longitudinally including the proportion of T cell subsets in circulation. This study also profiled immune checkpoint expression on circulating T cells including: PD-1, CTLA-4, TIGIT, TIM-3, LAG-3, PD-L1 and PD-L2. Markers of immunogenicity (calreticulin, HMGB1 and MIC-A/B) were also assessed.

Results: The frequency of naïve T cells increased in circulation from POD-0 to POD-7 ($P<0.01$) but returned to baseline at week 6. Effector memory T cells decreased by POD7 ($P<0.01$) returning to normal by week 6. Increases in activated circulating CD27+ T cells was observed from POD-0 to POD-7 ($P<0.01$), interestingly remaining high

in a proportion of patients that experienced complications. The percentage of immune checkpoint positive T cells peaked on POD-1 and was substantially decreased by week 6 ($P<0.01$).

Conclusions: We observed increased T cell activation and immune checkpoints immediately post-surgery with returns to baseline by week 6. These results suggest that ICIs such as anti-PD-1 may be beneficial immediately post-surgery to maintain T cell activation and prevent exhaustion of this increased population of activated T cells observed immediately post-surgery.

Keywords: Major oncological resection; immunosuppression; immune checkpoints; T cell activation; oesophageal adenocarcinoma

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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