

AB178. SOH21AS195. The importance of the lymph node: incorporating clinicopathological features with immunological modulation in tailored multimodal treatment for oesophageal adenocarcinoma

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Background: There is a need to develop a deeper understanding of the tumour microenvironment (TME) and tumour-draining lymph node microenvironment (LNME) to inform novel therapeutic approaches. Our study profiles the immune, angiogenic and inflammatory environment of the LNME and the TME of oesophagogastric patients.

Methods: Immune checkpoints (ICs) on tumour-draining lymph nodes (TDLNs, n=6) and tumour tissue (n=9) at surgical resection was assessed by flow cytometry. We also screened for cytokines, angiogenic mediators and chemokines. Using The Cancer Genome Atlas (TCGA), protein and mRNA levels (n=72) and mutated versus non-mutated copies (n=87) of this panel was correlated with survival.

Results: The frequency of CD3 + TIM-3 + and CD3 + PD-1 + T cells in TDLNs positively correlated with clinical tumour as did CD8 + PD-1 + and CD8 + TIGIT + T cells with nodal metastasis. Pro-angiogenic factor bFGF was significantly higher within the TME compared with the LNME. PIGF and SAA mediators of tumour growth were significantly higher in the LNME and levels of SAA in LNME positively correlated with adverse features. High

levels of pro-inflammatory IL-8, IL-6 and Flt1, mutations in pro-inflammatory genes CCL26, IL-31 and IL-17C and anti-tumour IL-1RN and CCL22 correlated with reduced overall survival.

Conclusions: The TME is more immunosuppressive than the TDLN, however, certain pro-angiogenic factors were enriched in TDLNs suggesting the priming of a pre-metastatic niche. Given the association of ICs including PD-1, TIM-3 and TIGIT within the TME and LNME with tumour stage and nodal involvement these may be promising therapeutic targets.

Keywords: Nodal burden; immune checkpoints (ICs); oesophageal adenocarcinoma; neoadjuvant therapy; The Cancer Genome Atlas (TCGA); cytokines; chemokines

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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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