AB065. 137. Clinically relevant chemotherapies promote immune resistance via upregulation of inhibitory immune checkpoints on T-cells and oesophageal adenocarcinoma cells

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Background: This novel study examines the expression of inhibitory immune checkpoints (IC) in oesophageal adenocarcinoma (OAC) to identify potential ICs that could be targeted as more than two-thirds of patients do not benefit from chemoradiotherapy (CRT). Importantly the effect of clinically relevant chemotherapies on the expression of ICs is examined to provide insight for rationally incorporating immune checkpoint inhibitors (ICIs) into current standards of neoadjuvant care for OAC patients.

Methods: Expression of PD-1 on tumor-infiltrating T-cells and peripheral blood T-cells in OAC patients was determined by flow cytometry. Activated T-cells and OAC cells were treated respectively, with single agent chemotherapy and IC expression was determined by flow cytometry.

Results: CRT significantly decreases PD-1 expression on peripheral blood and tumour-infiltrating T-cells in OAC patients ($P<0.05$). Single agent chemotherapy significantly increases PD-L1, PD-L2, CD160, TIGIT, PD-1 and LAG-3 on live activated T-cells ($P<0.05$). PD-1, CD160 and TIGIT are basally expressed on OAC cells ($P<0.05$). Single agent chemotherapy significantly upregulates PD-L1, PD-L2, TIM-3, LAG-3 and VISTA on live OAC cells ($P<0.05$).

Conclusions: ICs were identified on the surface of OAC cells which could potentially be targeted in OAC. This data also shows that chemotherapy affects the surface expression of ICs on OAC cells and T-cells highlighting a link between chemotherapy and immune resistance providing a rationale for combining ICIs with chemotherapy regimens in OAC. This data offers a starting point for understanding changes in IC expression in OAC which could help guide the selection and timing of ICIs with current standards of care to identify the best scheduling regimen for OAC patients.

Keywords: Immune checkpoints; oesophageal adenocarcinoma (OAC); chemotherapy

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