



AB072. Elucidating the role of radiation in altering the immunosuppressive tumour microenvironment in oesophageal cancer: a translational approach

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Background: The tumour microenvironment (TME) is closely connected to every step of tumourigenesis and increasing evidence suggests an active role of the TME in immune evasion. There is still a poor understanding on how radiation can modulate the tumour microenvironment.

Methods: Using an inhouse developed radioresistant oesophageal cancer cell line (OE33R) and age matched parental line (OE33P) we emulated the harsh conditions of the TME by culturing cells in conditions of mild and severe hypoxia and nutrient deprivation. In addition, we also used age matched healthy donor and cancer patients peripheral blood mononuclear cells (PBMCs) and cultured these under nutrient deprivation. These cells were then treated with bolus (2, 10 Gy) or fractionated radiation (3x2 Gy,

3x4 Gy, 3x8 Gy). The effects of radiation on the expression of immune checkpoints (IC) TIGIT, PD-1 and its ligands PD-L1, PD-L2 and damage associated molecular patterns (DAMPs) calreticulin, HMGB1 and MIC A/B was then evaluated by flow cytometry.

Results: In the OE33P & R cells, both standard and nutrient deprivation conditions resulted in a significant increase in immune checkpoint (IC) and DAMP expression under normoxia following fractionated and bolus dosing ($P<0.01$) with 3x4 Gy and 3x8 Gy resulting in the highest expression ($P<0.001$). In OE33R cells, while expression of IC's and DAMPs were lower in mild (5%) and severe (0.5%) hypoxia compared to normoxic conditions, 3x4 Gy, 3x8 Gy and 10 Gy treatment regimens resulted in increased IC and DAMP expression ($P<0.01$) In OE33P cells severe hypoxia resulted in a significant decrease in expression of both IC's and DAMP's compared to normoxia ($P<0.001$).

Conclusions: The increased expression of IC's particularly immunosuppressive PD-L1 and PD-L2 suggest that current fractionated radiation treatments of 2 Gy is not optimal for combination with immunotherapy in oesophageal cancer.

Keywords: Radiotherapy; oesophageal cancer; immunotherapy; tumour micro environment; immunosuppression

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