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**Multiomics analysis of immune correlatives in hepatocellular carcinoma patients treated with tremelimumab plus durvalumab**

**Myojin Y, Babaei S, Trehan R, et al. Multiomics analysis of immune correlatives in hepatocellular carcinoma patients treated with tremelimumab plus durvalumab. Gut 2025; 74(6): 983-995. doi: 10.1136/gutjnl-2024-334026.**

Immunotherapy with combined checkpoint inhibitors such as tremelimumab (anti-CTLA4 (Cytotoxic T-lymphocyte associated protein 4)) with durvalumab (anti-PD-L1 (Programmed death-ligand 1)) has become a standard treatment option for advanced HCC (Hepatocellular carcinoma). Myojin et al., performed a multiomics analysis (whole exome sequencing, single cell RNA sequencing, CO-Detection by indexing (CODEX), multicolour spectral flow cytometry and cytokine/chemokine analysis) of 28 patients treated with this regime and combination locoregional therapies as part of a Phase II clinical trial. The aim was to characterise the immune profile of the HCC tumour microenvironment and identify potential biomarkers of response.

They compared responders (n=13) vs. non-responders (n=15) defined as progression free survival greater vs. less than 6 months. Differentially expressed gene analysis revealed increased CXCL9 (Chemokine ligand 9) and CXCL10 (C-X-C motif chemokine ligand 10) in responders. Gene set enrichment analysis showed inflammatory pathway upregulation in responders with enhanced interferon signatures.

Spatial analysis found increased T regulatory cells in non-responder tumours with higher levels of PD-1 expression. In the peripheral blood there was increased Tregs (regulatory T cells) in non-responders compared to higher monocytes in responders. Myojin et al., used a pre-clinical mouse model where mouse liver cancer cell lines were injected into livers of C57/BL6 mice. There was enrichment for Tregs in the tumours of mice with progressive disease. Myojin et al., concluded that Treg distribution was important in HCC treatment response.