PROGNOSTIC BENEFIT OF TUMOR-INFILTRATING LYMPHOCYTES IN PATIENTS WITH HIGH GRADE SEROUS OVARIAN CANCER IS DEPENDENT ON TREATMENT REGIMEN, SURGICAL OUTCOME AND T CELL DIFFERENTIATION

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Tumor-infiltrating lymphocytes (TIL) are associated with a better prognosis in high grade serous ovarian cancer (HGSC). However, it remains largely unknown how this prognostic benefit of TIL relates to current standard treatment of surgical resection and (neo-)adjuvant chemotherapy. To address this outstanding issue, we compared TIL infiltration in a unique cohort of advanced stage HGSC patients primarily treated with either surgery or neo-adjuvant chemotherapy.

Tissue Microarray (TMA) slides containing samples of 171 patients were analyzed for CD8+ T cell infiltration by immunohistochemistry. CD8+ T cell subsets in freshly isolated TIL were characterized by flow cytometry based on differentiation, activation and exhaustion markers. Relevant T cell subset markers were validated using immunohistochemistry (TMA) and immunofluorescence (full slides).

A prognostic benefit for patients with high intratumoral CD8+ TIL was observed if primary surgery had resulted in a complete cytoreduction (no visible tumor present). By contrast, optimal (<1 cm of remaining tumor) or incomplete cytoreduction fully abrogated the prognostic effect of CD8+ TIL. Subsequent analysis of primary TIL by flow cytometry and immunofluorescence identified CD27 as a key marker for a naïve-like, yet antigen-experienced and potentially tumor-reactive CD8+ TIL subset. In line with this, CD27+ TIL remained associated with an improved prognosis even in incompletely-cytoreduced patients. Finally, neither CD8+ nor CD27+ cell infiltration was of a prognostic benefit in patients treated with neo-adjuvant chemotherapy.

Our findings indicate the treatment regimen, surgical result and the differentiation of TIL should all be taken into account when studying immune factors in HGSC or, by extension, selecting patients for immunotherapy trials.