57 ASSESSMENT OF THE SPATIAL DISTRIBUTION OF B CELLS SUBPOPULATIONS IN THE TUMOR MICROENVIRONMENT AND TERTIARY LYMPHOID STRUCTURES BY BRIGHTPLEX®, A SEQUENTIAL CHROMOGENIC MULTIPLEX ASSAY

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Background Density and localization of T cells within the tumor microenvironment (TME) is critical to control tumor growth. Immunotherapy with antibodies against immune checkpoint inhibitors (ICI), which aim to reinvigorate exhausted T cells, despite inducing long-term response in many cancer types, remains ineffective for most patients. Other factors present in the TME may participate in the control of tumors, among several candidates, the role of B cells has been underestimated. Publications revealed that B-cells are associated with good prognosis in several indications. However, there are no general rules since neutral or even deleterious impact of the presence of B-cells in the tumor was reported. Among other hypotheses, we can suppose that the level of activation and isotype switch will be important to mediate activation of NK cells or ADCC within the tumor and will have a favorable impact on the prognosis. In addition, the spatial distribution of B-cells may be important since, in the TME, they are mostly located in Tertiary Lymphoid Structures (TLS) which are ectopic lymphoid organs. Mature TLSs contain zones where dendritic cells (DC) present antigen to T-cells and others where proliferating B-cells undergo class switch and maturation toward plasma cells. Antigen presentation by B cells to T cells is supported by DCs, therefore, the presence of these three types of cells within the TLS allows T cell activation in the TME. If B-cells are major players in the therapeutic efficacy of ICI antibodies, not all subtypes of tumor infiltrating B-cells are likely to participate in response to immunotherapy.

Methods To decipher the roles of B cells, new tools are needed to identify the differentiation and activation status of individual B cells. We have developed a 7-plex panel of antibodies against biomarkers that allow the identification of main types of B cells.

Results On a single FFPE tissue section: naïve, unswitched memory, switched memory, activated, plasmablast and plasma B cells, as well as T cells and DC are identified. Following images registration, complex cells phenotypes can be detected and quantified. Furthermore, digital pathology tools allow the evaluation of the spatial distribution within the TME of subtypes of B cells especially in association with TLSs.

Conclusions This new tool unravels the heterogeneity of B cells in TME and could help clinical researchers to understand their contribution to the response to immunotherapy. Integrated into an Immunogram, this new Brightplex® Panel will be critical to understand the immune contexture of the tumor.

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