ABSTRACT FORM

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ABSTRACT TITLE Gene expression profiling (GEP) and tumor immune microenvironment analysis of extensive small-cell lung cancer (eSCLC) patients receiving first-line platinum-etoposide plus atezolizumab (PEA)

Background: First-line systemic treatment with PEA is a new standard of care for eSCLC. No predictive biomarkers for patient selection have been identified so far.
Methods: This is a single-center prospective translational study on eSCLC patients receiving first-line PEA, investigating the predictive value of tissue biomarkers. GEP was performed analyzing 770 immune/cancer-related genes by the Nanostring® PanCancer IO360 panel, while a 9-color multiplex immunofluorescence (mIF) panel was used to quantify immune cell distribution and their spatial relationships. Gene expression signatures and immune cell densities and interactions were correlated with efficacy and activity endpoints.
Results: Twenty patients were included; median follow-up was 12.8 months. Overall response rate was 63%, median time to treatment failure (TTF), progression free (PFS) and overall survival (OS) were 5 (95% CI, 3.9-6.1), 5 (95% CI, 3.9-6.1) and 7.2 months (95%CI, 7.1-7.4), respectively. A differential expression of genes coding for costimulatory molecules and cytokines/chemokines were reported between responders and non-responders, and in patients with longer versus shorter PFS. A lower cytotoxic T-cell (CTL)/tumor-infiltrating lymphocytes (TILs) signature score ratio (ssr) was associated with shorter OS, PFS and TTF. High T-cells/TILs, mast cells/TILs ssr and low macrophages/TILs ssr were associated with better outcome. At mIF analysis, responders had a higher percentage of intra-tumoral T regulatory (Treg) cells and a lower percentage of intra-tumoral CD68+CD163+ tumor-associated macrophages (TAMs) compared to non-responders. Moreover, higher percentages of HLA-I+ tumor cells and Treg cells close to CTL were observed in responders. Higher densities of CD8+ T lymphocytes and stromal B cells, and a higher percentage of tumor or B cells close to CTL were associated with a better OS. A longer PFS and TTF were observed in patients with lower TAMs density and with a higher percentage of tumor or CTL in contact with TAMs. Moreover, the lower TAMs/TILs ratio and a higher percentage of Treg cells in contact with CTL was associated with a longer OS, PFS and TTF, as well as a higher percentage of CD68+CD163- macrophages within a 25 µm radius from CTL.
Conclusions: We identified predictive and prognostic immune signatures, immune cell populations and cell-to-cell interactions in eSCLC receiving chemo-immunotherapy through GEP and spatial mIF analyses. These data will be confirmed in a wider validation set of patients with a longer follow-up and complemented with circulating biomarkers analysis.

KEYWORDS: Tumor and Stromal targeting, Immunotherapy

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