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Immune microenvironment in classical Hodgkin lymphoma: Composition and dynamics in patients with relapsed/refractory disease

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Background

Classical Hodgkin lymphoma (cHL) is characterized by the unique tumor microenvironment (TME) rich in immune cells. One of the explanations for the depressed antitumor response in cHL is hyperexpression of inhibitory immune checkpoint receptors on T cells as well as increased proportion of M2 macrophages (M2) in TME. The presence of high number of M2 has been demonstrated to worsen the prognosis of patients treated with standard chemotherapy, while data regarding the prognostic value of TME features in patients treated with PD-1 inhibitors is limited.

Methods

This retrospective study included 61 primary tumor samples from pts with r/r HL, treated with Nivo, and 15 repeated samples obtained during relapse or progression of disease after immunotherapy. The PFS and the best overall response (BOR) depending on the proportion of cells positive for CD68, CD163, PD-1, LAG-3, TIM-3, CTLA-4, TIGIT, c-MAF in the TME in primary and sequential biopsies were analyzed. Immunohistochemical staining was performed with Bond III (Leica Biosystems). The antibody cocktail (CD163/c-MAF) was used for identification of M2. The response to Nivo was assessed by PET-CT with LYRIC. ROC analysis established 8,5% cut-off value for CD163 expression and 11,5% for CD68 expression, dividing patients with high and low number of positive cells.

Results

In the CD163low group, 4-year PFS was 24,1% (95% CI 9,3%-42,6%) with a median PFS of 11,6 months (95% CI 7,2-24,8); in the CD163high group - 42,6% (95% CI 20,2%-63,4%) with a median of 24,8 months (95% CI 20,4 - NA), p = 0,0086. Complete remission (CR) achievement as BOR to Nivo was associated with a lower level of M2 in primary biopsies (p = 0.047). In the analysis of sequential samples, an increase of PD- 1+ and LAG-3+ T-cells and depletion of CD68+ and CD163+ cells in repeated biopsies was observed (median PD-1–1.0% vs 7.0%; LAG-3–5.0% vs 8.0%; CD68–10.0% vs 7.0%; CD163–9.0% vs 3.0%, p<0,05).

Conclusions

We found that low number of CD163+ cells in primary samples were associated with inferior PFS during Nivo therapy, while a lower level of M2 was correlated with achievement of CR. In repeated biopsies after Nivo therapy the cell profile in the TME changed: number of PD-1+ and Lag-3+ T-cells increased and number of CD68+ and CD163+ macrophages decreased.

Legal entity responsible for the study

Liudmila Fedorova.

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Disclosure

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