Depletion of T lymphocytes is correlated with response to temozolomide in melanoma patients - DTU Orbit (17/12/2018)

Depletion of T lymphocytes is correlated with response to temozolomide in melanoma patients

Therapeutic strategies to deplete lymphocytes, especially regulatory T cells, in cancer patients have been proposed to increase the benefits of (immuno) chemotherapy. In this study, we explored the influence of temozolomide (TMZ) on different T-cell populations and addressed if the depletion of CD4(+) T cells would be associated to the clinical benefits of TMZ. Patients were treated with TMZ (150 mg/m(2) daily, every two weeks on a 4-week schedule) until disease progression. Changes in T-lymphocyte subsets were characterized by flow cytometry. All patients enrolled in this study had histologically verified unresectable Stage IV melanoma. Objective responses were induced in 12.5% of the patients, while 42.5% of them obtained short-term disease stabilization. The median progression-free survival (PFS) of this patient cohort was 8.7 mo. Lymphopenia (<0.7 x 10(9) cells/L, grade 2) developed in 71% of the patients after 3 treatment cycles (similar to 100 d). The development of grade 2 lymphopenia after the 3rd cycle of therapy positively correlated with clinical outcome (p = 0.01), and was linked, though non-significantly, to prolonged median PFS (303 vs. 200 d). In addition, significant changes in CD8(+) T-cell subgroups were observed, notably a shift from naive T cells toward more differentiated memory T cells. Finally, we demonstrated that specific CD8(+) T-cell responses against selected tumor associated antigens (TAAs) were enhanced by the administration of TMZ (p = 0.04), while virus-specific T-cell responses were stable. Thus, immunological monitoring in the course of TMZ treatment might become an important tool for clinical guidance in the future.

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