Peripheral Regulatory T Cells are Expanded but do not Impact Survival in Newly Diagnosed Glioblastoma

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Introduction

Regulatory T cells (Tregs) have an immunosuppressive function that can promote tumor growth in numerous malignancies. Prior studies have shown that Tregs as a fraction of the CD4+ T cell population are expanded within the tumor microenvironment and peripheral blood of GBM patients. Differing studies have shown mixed associations between the presence of intratumoral Tregs and GBM patient survival. Although circulating Tregs have been shown to impact survival in preclinical models of GBM, no clear association has been demonstrated clinically in patients. Here, we investigate the clinical impact of peripheral Treg expansion in newly diagnosed GBM patients receiving standard treatment.

Methods

Peripheral blood leukocytes were isolated from 61 newly diagnosed GBM patients prior to surgery. Tregs (CD4+CD25+FoxP3+) were quantified by flow cytometry, and patients were divided into Treghi and Treglo subsets relative to the median. All patients underwent maximal safe resection followed by standard chemoradiation. Radiographic progression and overall survival were recorded.

Results

Peripheral Treg populations ranged from 0.3-14.3%, with a mean of 4.5%. Median progression free survival (PFS) for all patients was ¬¬9.5 months and median overall survival (OS) was 14.8 months. PFS for the Treghi and Treglo groups was 9.0 and 11.2 months, respectively (HR = 0.91; p=0.77). OS for the Treghi and Treglo groups was 14.8 and 16.1 months, respectively (HR = 0.95; p=0.89). Patients in the bottom quartile were compared to the top quartile without statistically significant differences in PFS (HR = 0.64; p=0.33) or OS (HR = 0.58; p=0.24).

Conclusions

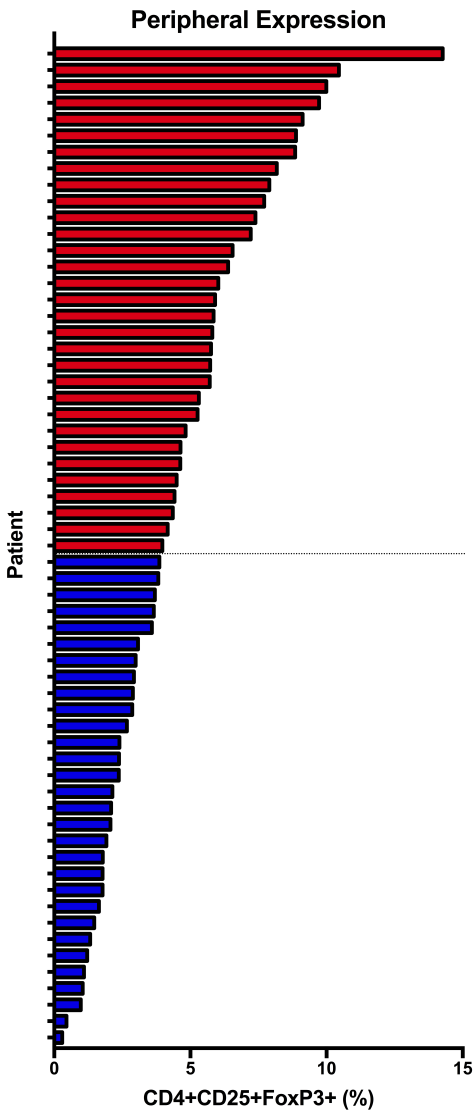
In patients receiving standard of care treatment for newly diagnosed GBM, Treg expansion in peripheral blood does not significantly impact survival. As the use of immune checkpoint targeting therapies, including the Treg targets CTLA-4 and CD25, are increasingly used in the management of cancer, these findings should be strongly considered when designing studies for GBM.

Learning Objectives

By the conclusion of this session, participants should be able to:

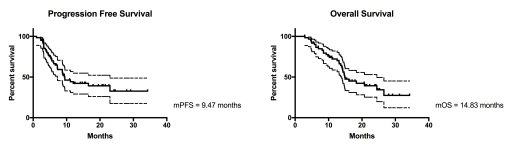
1) Describe the importance of Treg

Figure 1. Peripheral Treg Expression



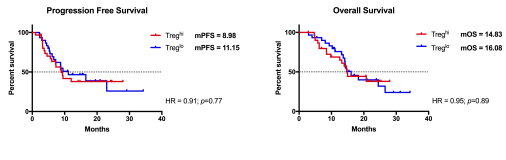
Peripheral Treg abundance was analyzed by flow cytometry for 61 patients with newly diagnosed GBM. Populations ranged from 0.3-14.3%, with a mean of 4.5%.

Figure 2. Progression-Free and Overall Survival for All Patients



Patients with quantified peripheral Treg expression were followed through the treatment course. Median progression free survival (PFS) for all patients was 9.5 months, and median overall survival (OS) was 14.8 months.

Figure 3. Impact of High versus Low Treg Expression on Outcomes



Patients were divided into Treg(hi) and Treg(lo) subsets relative to the median. PFS for the Treg(hi) and Treg(lo) groups was 9.0 and 11.2 months, respectively (HR = 0.91; p=0.77). OS for the Treg(hi) and Treg(lo) groups was 14.8 and 16.1 months, respectively (HR = 0.95; p=0.89).