

Activation of immune response in refractory patients to standard treatment (T.R.A.N.S.L.A.T.E.)

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Purpose/Objectives: The TRANSLATE project started in 2016 to test the immune effects of metronomic cyclophosphamide, daily low-dose IL-2 every other week, and a single flash of radiotherapy (RT) in peripheral blood. The rationale is based on self vaccination induced by radiotherapy (RT) 8 Gy single fraction on one metastatic lesion, T cells expansion by IL-2 treatment and selective Tregs down regulation by lowdose cyclophosphamide administration.

Materials/Methods: We enrolled patients with end-stage breast, colon, kidney and prostate cancer. Analysis was performed at baseline, the day after RT, after 28 days from treatment start and at disease progression. Assay focused on Tregs, CD8+, NK, MDSC, CD3-PD1, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, IL-13, IL-17a, TNF α , IFN γ , TGF β . We divided patients into two groups depending on the time of disease progression (A > 3 months; B, < 3 months). We report preliminary data with the aim to show the changes observed post-RT in 20 pts.

Results: At baseline, group B had higher rates of CD3-PD1, higher IL-2, IL-13, TNF α , and TGF β ; group A had higher IFN γ , IL-4, and IL-12. After RT, we observed a difference between the two groups in the rates of CD3-PD1 (lower in group B) and Tregs (higher in group A). Among cytokines, only TNF α reached a statistical significance (higher in group B). We also observed that TGF β and IL-6 were higher in group B and IFN γ was higher in group A. The longitudinal analyses showed that CD3-PD1 remained stable between basal and post-RT in group A but decreased in group B. Tregs marginally increased in group A. TNF α , TGF β , IL-4, IL-6, and IL-12 increased in group B. IL-4 decreased in group A and IL-6 and IL-12 also marginally decreased in the same group. IFN γ slightly increases in group A.

Discussion: The limited number of patients reduced the interpretation of the study. However, following RT a positive trend of Th2 cytokines is observed in patients with early progressing disease, without the expected surge of IFN γ that was instead observed in patients with better outcome. Additional analyses are in progress and will be presented.