Biomarker analysis in localized urothelial cancer DUART patients post-treatment.

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Background: Patients with localized unresectable or cisplatin-ineligible urothelial cancer (UC) have limited treatment options. Biomarker identification can guide targeted therapies. In the DUART study, pre-treatment immune cell subsets were significantly linked to disease control. Our planned correlative aim was to evaluate the same biomarkers using post-adjuvant treatment (post-Rx) peripheral blood mononuclear cells (PBMCs). **Methods:** This was a prospective, multi-institutional study BTCRC-GU15-023. Our N=16 all had valid Post-Rx values and disease control status. Eligibility criteria: >18yrs, advanced/unresectable UC, and available tumor specimen. All received concurrent durvalumab and radiation therapy followed by adjuvant durvalumab in a Phase II study. Blood samples were taken at pretreatment, 12 weeks, and post-Rx. Biomarkers were detected using multicolor flow cytometry-based analysis of PBMCs to detect T lymphocyte subsets and by dimensionality reduction using FlowJo. *Correlative objective: Evaluate post-Rx time points for biomarkers that contribute to disease progression or response.* Two-sample T-tests were used to study the association. All tests were two-sided and the statistical significance level used was 0.05. **Results:** Standard flow cytometry analysis revealed a statistically significant increase in ICOS+ CD4 and CD8 T cells in post-Rx samples among patients with progression-free survival at one year. In addition, responder patients (CR/PR/SD, n=12) showed a significant decrease in CD8 central memory T cells compared to progressors (PD, n=4) in post-Rx samples. Although not statistically significant, additional trends were noted, including decreased PD-1+ CD4 T cells in responder patients, decreased CD4 T effector memory RA+ (TEMRA), and increased CD4 naïve T cells in responder patients. There was a slight increase in interferon gamma-producing CD8 T cell subsets in responder patients and a significant decrease in central memory CD8 T cells. tSNE analysis revealed similar trends in the data, including increased naïve CD4 T cells in responder patients and slight increases in some cytokine-producing CD8 T cell subsets. **Conclusions:** Our small cohort demonstrates some significant differences in post-Rx T cell populations linked to therapy response, and further evaluation in a larger cohort of patients is needed. The identification of predictive biomarkers could help a more personalized therapeutic approach. Research Sponsor: AstraZeneca.