Assessment of tumor antigen specific T cell immunity and cytokine milieu at diagnosis in patients with high risk Hodgkin Lymphoma treated on Children's Oncology Group trial AHOD1331

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On behalf of The Children's Oncology Group

Introduction

The role of the immune system and the microenvironment in classical Hodgkin Lymphoma (cHL) has been established. However, little is known about the baseline plasma cytokine profile and tumor antigen specific T cell responses in pediatric and adolescent and young adults (AYA) patients. We examined the feasibility of evaluating tumor specific T cell responses and cytokines at diagnosis in children and AYA on a Phase III trial.

Methods

AHOD1331 (NCT02166463) randomized newly diagnosed high risk cHL patients 2-21 years of age to standard or brentuximab containing chemottherapy. Between March 2015 and August 2019, peripheral blood was obtained at baseline from 441 of the 600 enrolled patients. Mononuclear cells and plasma were isolated within 24-72 hours of blood collection using Ficoll Density gradient and cryopreserved. Non-adherent T cells were stimulated *ex vivo* with autologous dendritic cells pulsed with HL specific pepmixes for the tumor associated antigens (TAA) MAGEA4, PRAME and Survivin and cultured in the presence of cytokines. T cell specificity to the TAAs was tested using Interferon-γ ELISPOT assay and considered positive if the number of spot forming counts (SFC) per 10^5 T cells was twice that of the control (Actin). Plasma samples were tested for 17 inflammatory cytokines using Luminex assay. Baseline immune response and cytokine levels were compared in univariate analysis for: age, gender, stage, B symptoms, bulk, EBER status and large mediastinal adenopathy.

Results

In the 72 patients evaluated to date for tumor antigen specificity, in vivo T cell responses were detected to at least one of the three non-EBV tumor associated antigens in 58%. The mean SFC/ 10^5 T cells for MAGEA4, PRAME and Survivin was 6.2 (95% 2.7-9.7), 13.2(95% CI 4.2-16.3) and 5.9(95% CI 2.4-9.5) respectively. T cell responses were associated with age >12 years(p=0.01) and higher stage (p=0.04).To date, 167 baseline plasma samples have been analyzed. Interleukin-10 was significantly elevated in patients < 12 years of age compared to >12 years(p=0.04) and mean Interleukin-5 levels were higher in

patients without bulky disease (p=0.02).

Conclusion

T cell responses to TAAs can be detected in patients with HL at diagnosis and differ by patient and disease factors. We are currently completing the cytokine analysis and T cell responses on all the patient samples received to date. Once completed, our study will provide baseline immune markers on one of the largest cohort of pediatric and AYA patients with HL.

Acknowledgment
No disclosures