Combinations of Immune Checkpoint Blockade Inhibitors and Lymphodepletion as Immunotherapy for Myeloma

Tlomak, Dominique

Multiple myeloma is a plasma cell neoplasm characterized by destructive bone lesions and currently has no cure. Successful treatment of multiple myeloma will require a multi-faceted approach incorporating drug therapy, immunotherapy and other novel strategies. The primary goals of the current year study were to determine if CTLA-4 specific antibodies accompanied by lymphodepletion and PD-1/PD-L1 blockade can increase T cell reactivity, use an Elispot analysis to determine if the immune response against multiple myeloma is occurring as a result of antibody treatment, and determine the most efficient and least aggressive combination therapy for treating multiple myeloma using immunotherapy techniques. My study showed that the anti-myeloma effect of transient lymphodepletion and PD-1/PD-L1 blockade is increased by adding other checkpoint blockade inhibitors, specifically CTLA-4 antibody treatment. This is important because CTLA-4 has been approved by the Federal Drug Administration for clinical use in malignant melanoma patients. It is the first immune checkpoint blockade therapy to be approved. CTLA-4, in addition to anti-PD-L1 and lymphodepletion was associated with increased T cell reactivity and as a result an increased anti-myeloma effect, which were confirmed by Elispot analysis. Elispot analysis indicated increased immune checkpoint protein expression (PD-L1, PD-L1+TIM-3, PD-L1+LAG-3, PD-L1+CTLA-4) on tumor specific T cells. This data supports the hypothesis that partial lymphodepletion and immune checkpoint protein blockade is a promising strategy in combating multiple myeloma and other hematologic malignancies.

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