



Immunotherapy and Clinical Trials for Uveal Melanoma
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Dr. Kammula presented the following research at the 2016 Society for Melanoma Research Congress CURE OM Scientific Meeting and will provide an update at the Eyes on a Cure: Patient & Caregiver Symposium on March 10-11, 2017 in Washington, DC.

Uveal melanoma is the most common primary malignancy arising within the adult eye. Overall, however, this is a rare cancer with an annual incidence of ~6 per million in the U.S, accounting for 3.7% of all melanomas. These tumors originate within the pigmented uveal tract (which include the choroid, ciliary body, and iris) and are notable for characteristic cytogenetic changes, oncogenic mutations in GNAQ or GNA11, and an unusual predilection to aggressively metastasize to the liver resulting in a dismal prognosis. Although a variety of immune based therapies have demonstrated efficacy in metastatic melanoma of cutaneous origin, their use in uveal variants has been disappointing, thus far. These findings have led to speculation that melanomas arising within the eye may represent an immunotherapy resistant variant.

Recently, however, we discovered an immunogenic subset of uveal melanoma based upon laboratory studies of tumor infiltrating lymphocytes (TIL) isolated from freshly resected liver metastases. In our current clinical trial (registered with ClinicalTrials.gov as NCT01814046), we sought to determine if infusion (also called adoptive transfer) of such TIL could mediate cancer regression in metastatic uveal melanoma patients, especially after prior immunotherapy failure. Adoptive T cell therapy using autologous TIL has been reported to induce salvage responses in a variety of refractory solid tumors with durable and complete regression in some of these patients. However, the efficacy of TIL therapy in uveal melanoma patients has not been formally investigated.

Thus far, we have enrolled twenty-one metastatic uveal melanoma patients on this single center phase 2 trial at the NIH. All patients were treated with infusion of autologous TIL and high-dose interleukin-2 after lymphodepleting conditioning chemotherapy. Seven of 20 (35%) evaluable patients demonstrated objective tumor regression. Among the responders, six patients achieved partial tumor regression, two of which are ongoing and have not reached maximum response. One patient achieved complete tumor regression currently ongoing at 21 months post therapy. Three of the responders were refractory to prior immune checkpoint blockade.

Our findings demonstrate, for the first time, the ability of adoptive transfer of autologous TIL to mediate reproducible and durable complete tumor regression in patients with metastatic uveal melanoma. These results suggest adoptive T cell transfer to be an encouraging treatment option for this highly refractory disease. Refinement of this cell therapy is ongoing to further improve the frequency of these clinical responses.