366 COMPLETE TUMOR REGRESSION OF METASTATIC EPITHELIAL CANCER FOLLOWING T CELL RECEPTOR (TCR)-T CELL THERAPY

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Background Genetically engineered T cell therapy is highly effective for hematologic cancers. Development of the approach for common epithelial cancers has been more challenging. A phase I study of gene-engineered T cell receptor (TCR)-T cells targeting the HPV16 E7 oncoprotein (E7 T cells) for the treatment of metastatic HPV-associated cancers showed safety and clinical activity.[1] Here we report the interim results of a phase II clinical trial.

Methods Eligible patients had metastatic HPV16+ cancer from any primary tumor site and the germline HLA-A*02:01 allele. Treatment consisted of conditioning chemotherapy with cyclophosphamide and fludarabine followed by a one-time infusion of up to 50 billion E7 T cells and adjuvant high-dose systemic aldesleukin. The primary endpoint was overall response rate (complete + partial response) as measured by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Results Ten patients were treated at the time of the interim analysis. Patient characteristics included a median age of 60 (range, 30–63); primary cancer sites were head and neck (n=5), anus (n=2), cervix (n=2), and esophagus (n=1); and a median of 4 prior systemic anti-cancer agents (range, 1–6). Seven of 10 patients had previously received an immune checkpoint inhibitor. A median of 50 billion E7 T cells (range, 28–50 billion) and a median of 3 doses of aldesleukin (range, 2–6) were administered. The E7 TCR was expressed by a median of 80% (range, 76–94%) of the infused T cells. Grade 3/4 adverse events occurring in >1 patient were leukopenia (n=10), neutropenia (n=9), febrile neutropenia (n=8), anemia (n=5) and thrombocytopenia (n=5), consistent with the transient toxicities of conditioning chemotherapy and aldesleukin. Six of 10 patients demonstrated objective tumor responses (4 partial responses and 2 complete responses). Tumor responses were observed in head and neck (n=2), cervical (n=2), anal (n=1), and esophageal (n=1) cancers. Complete responses occurred in a patient with esophageal cancer previously treated with 3 agents, including pembrolizumab, and in a patient with anal cancer previously treated with 5 agents, including nivolumab. The duration of the complete responses is 8 months and 9 months, respectively, with both ongoing.

Conclusions At interim analysis, E7 T cells demonstrated safety and clinical activity, including complete tumor responses. The findings indicate that engineered T cell therapy can mediate complete regression of treatment-refractory metastatic epithelial cancers. Continued investigation of this treatment is warranted.

Trial Registration This trial was registered on clinicaltrials.gov, trial number NCT05686226.

REFERENCE

1. Nagarsheth NB, Norberg SM, Sinkoe AL, Adhikary S, Meyer TJ, Lack JB, *et al*. TCR-engineered T cells targeting E7 for patients with metastatic HPV-associated epithelial cancers. *Nat Med*. 2021 Mar;**27**(3):419–25.

Ethics Approval This study was approved by the WCG IRB; approval number CINJ 192204.

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