REAL WORLD DATA OF SEQUENCING IMMUNE CHECKPOINT INHIBITORS (ICI) AFTER INITIAL ICI

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Background ICI revolutionized modern Oncology landscape and being utilized in metastatic to adjuvant and neo-adjuvant settings. As Oncologists, we are treating cancer patients with ICI every day, yet there is still a lot that is unknown about these drugs. We don’t have clear understanding of the efficacy and toxicity when sequencing one ICI for another. We conducted a retrospective review of real world data at Lahey Hospital and Medical Center to understand further and pave path for prospective studies to understand this issue further to improve patient care.

Methods We retrospectively reviewed Oncology patient charts who received ICI between January 1, 2014 to December 18, 2018. Total 483 patients received ICI during this time frame and 22 of these patients received a second ICI either as monotherapy or in combination with other ICI or chemotherapy.

Results A total of 22 patients received subsequent ICI after the initial ICI as showed in table 1. 15 of the 22 (68%) patients were transitioned from one ICI to another monotherapy, 11 of these patients were transitioned secondary to disease progression (73%), three had immune related adverse events and one was switched per standard of care. One patient had ICI re-challenge. Three patients had a transition from ICI monotherapy to combination ICI therapy. One patient went onto chemo-immunotherapy and 2 patients transitioned from combination ICI to chemo-immunotherapy.

Conclusions ICI therapy is evolving and patients are being treated with multiple lines of ICI. In current practices, ICI is frequently being transitioned from cytotoxic T-lymphocyte antigen 4 (CTLA-4) and programmed cell death 1 (PD-1) or its ligand, programmed cell death ligand 1 (PD-L1) classes or combined with chemotherapy or targeted therapy. It would be prudent to explore the effects of sequencing these medications either as a monotherapy or in combination with other therapies to better serve our patients and to prevent financial toxicity.

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285 PHASE I CLINICAL TRIAL EVALUATING THE SAFETY OF ADP-A2M10 IN PATIENTS WITH MAGE-A10+ HEAD AND NECK, MELANOMA, OR UROTHELIAL TUMORS

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Background ADP-A2M10 SPEAR T-cells are genetically engineered autologous T-cells that express a high affinity MAGE-A10-specific T-cell receptor targeting MAGE-A10+ tumors in the context of HLA A*02. This trial is no longer enrolling (NCT02989064).

Methods This ADP-A2M10 dose escalation trial utilized a modified 3+3 design to evaluate safety and antitumor activity. Patients (pts) with advanced head and neck squamous cell carcinoma (HNSCC), melanoma, or urothelial cancer (UC) were enrolled. Pts were HLA A*02+ with tumors expressing MAGE A10. Pts underwent apheresis; T cells were isolated, transduced with a lentiviral vector containing the MAGE-A10 TCR, and expanded. Eligible pts underwent lymphodepletion with fludarabine and cyclophosphamide prior to receiving ADP-A2M10. ADP-A2M10 was administered at Dose Level (DL) 1 = 0.1 × 10⁶, DL2 = >1.2 - 6×10⁶, and Expansion = 1.2-15×10⁹ transduced cells.

Results As of January 10, 2020, 10 pts (8 male and 2 female) with HNSCC (4), melanoma (3), and UC (3) cancers were treated. Three pts each were treated at DL1 and DL2 and 4 pts were treated in Expansion. The most frequently reported adverse events ≥ Grade 3 were lymphopenia (10 pts), neutropenia (10), anemia (8), leukopenia (7), and thrombocytopenia (5). Two pts reported CRS (1 Grade 1, 1 Grade 3) with resolution. Responses included: 3 pts - stable disease, 5 pts - progressive disease, 1 pt - not evaluable, and 1 pt too early to determine. ADP-A2M10 SPEAR T-cells were detectable in peripheral blood from pts at each dose level and in tumor tissues from several pts at Expansion.

Conclusions There was no evidence of on- or off-target toxicity. Given the minimal antitumor activity and the discovery that MAGE-A10 expression frequently overlaps with MAGE-A4 expression, the clinical program has closed. Several trials with SPEAR T-cells targeting MAGE-A4 are ongoing (https://bit.ly/35htszK).

Trial Registration NCT02989064

Ethics Approval The trial was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines and was approved by local authorities. An independent ethics committee or institutional review board approved the clinical protocol at each participating center. All the patients provided written informed consent before study entry.

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