376 RADIATION SUB-STUDY TO CHARACTERIZE SAFETY AND TOLERABILITY OF LOW-DOSE RADIATION IN COMBINATION WITH AFAMI-CEL IN PATIENTS WITH ADVANCED CANCERS (NCT03132922)

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Background Autologous cell therapies with an engineered T-cell receptor targeting MAGE-A4 have shown responses in patients with synovial sarcoma[1] with additional responses in myxoid/round cell liposarcoma (MRCLS), head and neck, lung, esophagogastric junction, and melanoma cancers.[2 3] Low-dose radiation may control tumor growth locally and modulate stroma of solid tumors,[4] potentially facilitating T-cell infiltration into tumors and antitumor activity.

Methods Sub-study designed to assess safety, tolerability, and efficacy in up to 10 patients with low-dose radiation in combination with lymphodepleting chemotherapy, followed by afami-cel (an autologous TCR cell T-cell therapy targeting MAGE-A4). Eligible patients are HLA-A*02^+ with MAGE-A4 expressing tumors including urothelial, melanoma, head and neck, ovarian, non-small cell lung, esophageal, gastric, synovial sarcoma, and MRCLS cancers. Patients receive afami-cel by infusion following low-dose radiation and lymphodepleting chemotherapy. Radiation was 4.2–7 Gy per lesion or isocenter (maximum of 5). Lymphodepleting regimen was IV fludarabine 30 mg/m^2/day for 4 days (−7 to −4) and cyclophosphamide 600 mg/m^2/day for 3 days (−7 to −5). Afami-cel doses ranged from 1.2 x 10^9 to 10 x 10^9 transduced cells. Pts receive afami-cel infusion on Day 1.

Results As of Dec 27, 2020, a total of 8 patients, including 4 patients (1 male) with melanoma (2), HNSCC (1), or ovarian (1) cancers received low-dose radiation and afami-cel. Most frequently reported AEs (4/4 pts) were leukopenia/decreased white blood cell count, lymphopenia/decreased lymphocyte count, and neutropenia/decreased neutrophil count; all of which were related to the lymphodepletion regimen. The most commonly (>1 patient) reported AEs considered related to T-cell infusion were cytokine release syndrome (2/4 pts) and fatigue (2/4 pts). Two patients had a total of 5 SAEs: adrenal insufficiency, hyperglycemia, neurotoxicity, pneumonia aspiration, and pneumothorax. The only SAE considered to be related to treatment was Grade 3 neurotoxicity. Best overall responses per RECIST 1.1: 1 partial response (melanoma, −42% in target lesions), 2 stable diseases (ovarian cancer, −23%; HNSCC, no change), and 1 patient did not have post-baseline scans yet. Translational analyses showed peripheral persistence and serum cytokine response profiles consistent with that of afami-cel monotherapy, whilst a relatively greater T cell infiltration in tumor biopsies was evident.

Conclusions Afami-cel with low-dose radiation has had an acceptable safety profile. Most AEs were consistent with those typically experienced by cancer patients undergoing lymphodepletion cytotoxic chemotherapy and cellular therapy. Infused T-cells were observed in tumor biopsies at high frequency, and one patient exhibited a clinical partial response.

Trial Registration NCT03132922

REFERENCES

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