725 PRELIMINARY RESULTS OF A PROSPECTIVE PILOT STUDY USING CD8 IMMUNOPET IMAGING TO EVALUATE THE IMMUNE RESPONSE TO RADIATION THERAPY (ELIXR)

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Background Radiation therapy (RT) may produce immunomodulatory effects that can interact with immunotherapy. Our pilot study (NCT05371132) uses ^{89}Zr-Df-crefmirlimab, a radiolabeled CD8-specific minibody, to image intratumoral changes in CD8+ T cell activity during and after RT. Here, we present the results of our first four patients.

Methods Eligible patients have no change in systemic treatment within two months prior to RT and no splenic disorders. Patients receive a 1 mCi dose of ^{89}Zr-Df-crefmirlimab before and 1–2 weeks after a 5-fraction RT course. Each dose is followed by a whole-body positron emission tomography (PET) scan, and each radiation fraction is followed by a region-of-interest PET. Maximum standardized uptake values (SUV_{max}) of lesions are extracted from each CD8 ImmunoPET scan.

Results 3 metastatic renal cell carcinoma (mRCC) patients and 1 diffuse large B-cell lymphoma (DLBCL) patient have completed treatment. Median age was 64 years (range 61–65). Concurrent therapies included cabozantinib, nivolumab, and an experimental chemotherapy XL092 (table 1). The mRCC patients (P1-P3) received stereotactic body RT (30–40 Gy in 5 fractions) to one metastatic site. The DLBCL patient (P4) received RT (20 Gy in 5 fractions) to two lesions in the legs, in the bridging setting prior to chimeric antigen receptor (CAR) T-cell therapy. No toxicities attributable to the CD8 PET tracer were observed.

Mean peak increase in SUV_{max} of the treated lesion in P1-P3 was 14.5 ± 8.1 (standard deviation). Mean size reduction by longest diameter of P1-P3 was 36.3% ± 20.2% (standard deviation). Each patient's results are included in table 1. In P1, a normal lymph node saw an unusual 4.4 increase in SUV_{max} post-RT. At 8-month follow-up, this was found to have developed into a lesion (figure 1).

In P4, peak increase in SUV_{max} was 1.2 and 2.7 in the left and right leg treated lesions, respectively. Images are shown in figure 2. Two non-target lesions proximal to the left leg target lesion that received ~1% of the dose achieved an increase in CD8 SUV_{max} of 1.2 and 1.7 during radiation and resolved post-RT pre-CAR T. CD8 ImmunoPET taken 7 days post-CAR T infusion did not demonstrate any significant CD8 PET signal. All lesions resolved by day 30 post-CAR T on FDG PET imaging.

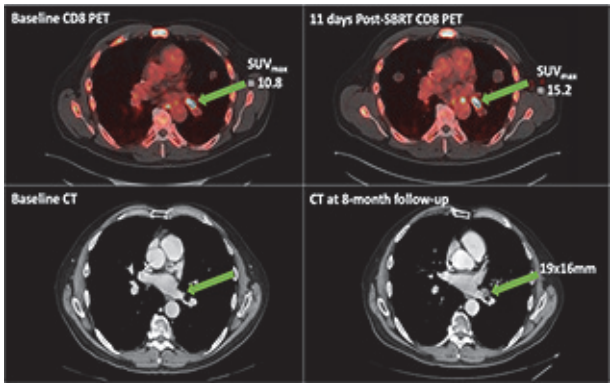
Conclusions Increase in intratumoral CD8+ T cell activity was observed during RT in mRCC and lymphoma patients. Follow-up may reveal the prognostic implications of visualizing the immunogenic effects of radiation using CD8 ImmunoPET.

Trial Registration NCT05371132

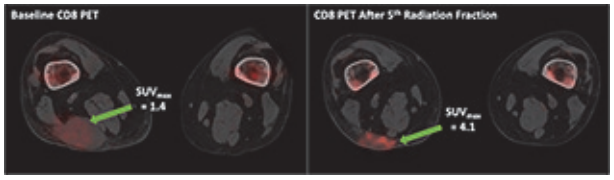
Ethics Approval This clinical trial was approved by the City of Hope Institutional Review Board (IRB) and has IRB number 21221. All trial participants provided informed consent prior to taking part in this study.

Abstract 725 Table 1 Change in CD8 ImmunoPET SUVmax of treated lesions and reponse

	Treated lesion site	Concurrent Therapy	Baseline SUV_{max}	Peak SUV_{max}	Timepoint of peak activity	Response to date
P1	Lung	XL092	1.3	5.2	4th RT fraction	47% decrease
P2	Right shoulder	Cabozantinib	6.8	19.0	Post-RT	13% decrease
P3	Subcarinal lymph node	Nivolumab	6.8	19.4	4th RT fraction	49% decrease
P4	Left leg	None	0.8	2.0	4th RT fraction	Resolved
	Right leg		1.4	4.1	5th RT fraction	Resolved



Abstract 725 Figure 1 Images showing a hilar lymph node that displayed notable increase in CD8 PET SUVmax post-radiation, which developed into a metastasis 8 months later



Abstract 725 Figure 2 CD8 PET imaging of the irradiated lesion in the right leg of a lymphoma patient who received bridging radiation before CAR T cell infusion

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