

# CD8 cell PET imaging with 89-Zr-crefmirlimab berdoxam (crefmirlimab) in patients with metastatic renal cell carcinoma (mRCC) receiving checkpoint inhibitors (CPIs): Association with response and tissue CD8 expression (4551).

Authors: Sumanta Kumar Pal<sup>1</sup> (SPal@coh.org), Przemyslaw Twardowski<sup>2</sup>, Delphine L. Chen<sup>3</sup>, Evan Thomas Hall<sup>3</sup>, David Hays<sup>4</sup>, Ian Wilson<sup>5</sup>, Kristin Schmiedehausen<sup>5</sup>, Michael Ferris<sup>5</sup>, William Le<sup>5</sup>, Michael A. Postow<sup>6</sup>;

<sup>1</sup>City of Hope, Duarte, CA; <sup>2</sup>John Wayne Cancer Institute, Santa Monica, CA; <sup>3</sup>University of Washington, Seattle, WA; <sup>4</sup>CARTI Cancer Center, Little Rock, AZ; <sup>5</sup>ImaginAb, Inglewood, CA; <sup>6</sup>Memorial Sloan Kettering Cancer Center, New York, NY

## Background &Methods

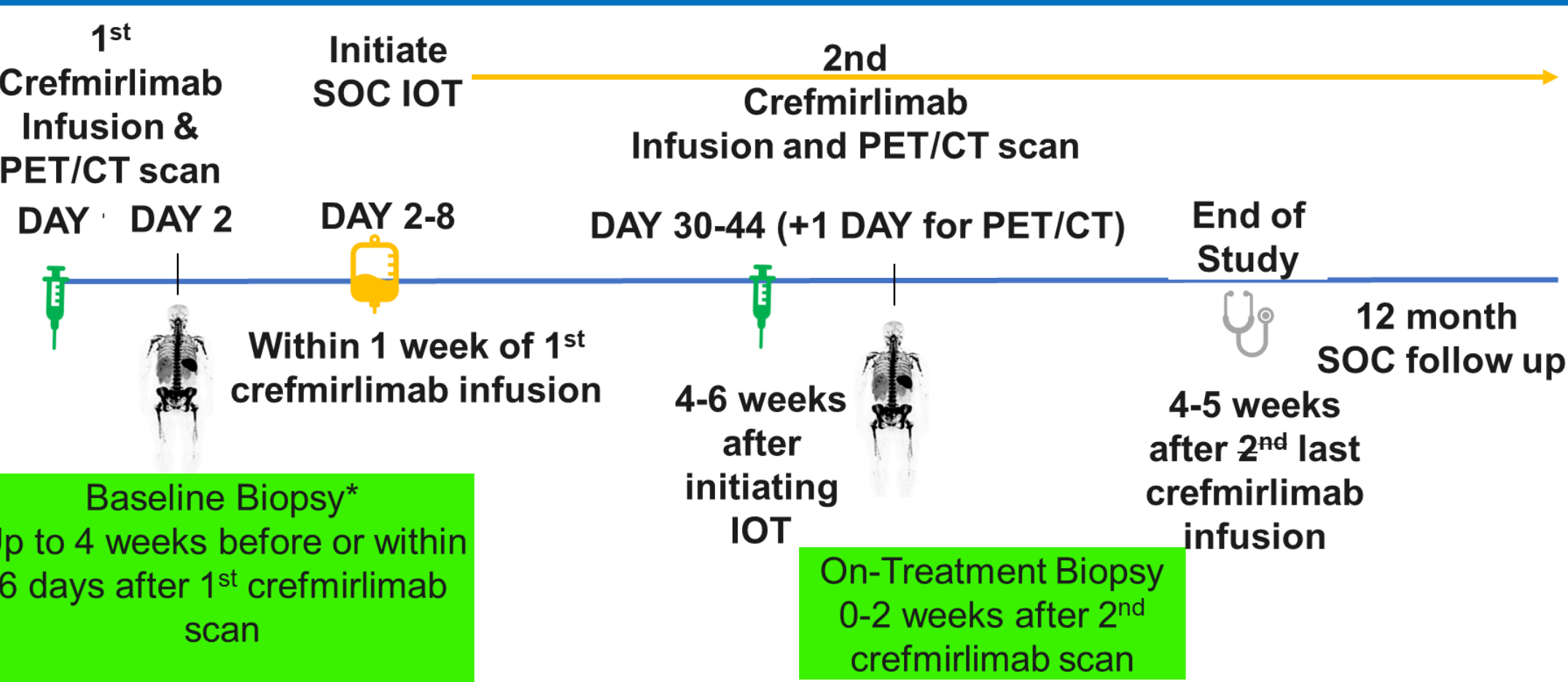
- In metastatic RCC (mRCC), no tissue-based biomarkers have been well established to predict outcome with contemporary regimens, e.g., checkpoint inhibitors (CPIs) or targeted therapy (TT)
- Herein, we present data from patients with mRCC in the iCorrelate Trial (NCT03802123), a study assessing crefmirlimab (a ~80 kDa <sup>89</sup>Zr-labelled minibody with high affinity for CD8) in patients receiving CPIs for advanced cancer
- We hypothesize that functional imaging of CD8+ T-cells crefmirlimab may predict response given the essential role of CD8+ T-cells in mediating CPI
- Eligible pts had pathologically verified RCC, metastatic disease and an intent to initiate standard of care CPI therapy
- Baseline biopsy was mandated, along with repeat biopsy 0-2 weeks following the second PET/CT scan.
- PET signal was characterized as SUV<sub>max</sub>, SUV<sub>peak</sub> and SUV<sub>mean</sub> of the biopsied lesions, uptake of reference tissues was quantified as well
- In addition, up to 5 index lesions and one representative CD8 avid lymph node per lymph node station were contoured and quantified
- Relationship between CD8 ImmunoPET uptake within the biopsied lesion and CD8+ cells/mm<sup>2</sup> by immunohistochemical staining (IHC) using the SP-57 antibody was assessed using the Spearman correlation coefficient
- The average SUV<sub>max</sub> of all contoured lesions in the CD8 PET was compared to the Best Overall Response according to RECIST 1.1 using the Wilcoxon Signed-Rank Test

## Patient Characteristics

Characteristic	Value	Characteristic	Value
Age, Median (range)	64 (54-71)	Sex	9 M: 8 F
Histology, N (%)		Best overall response*	
Clear cell	12(71%)	Response (CR or PR)	3(18%)
Unclassified	3(17%)	Non-response (SD or PD)	12(71%)
Papillary	2(12%)	Not evaluable	2(12%)

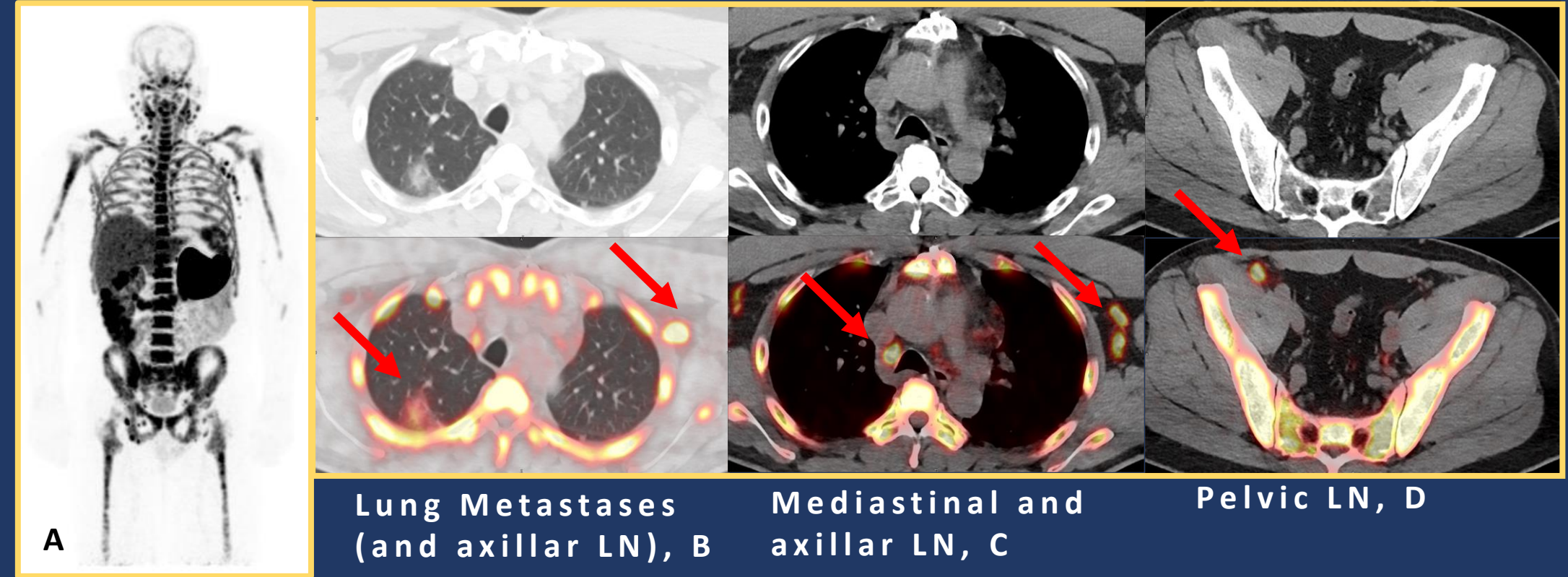
\*By RECIST v1.1. CR = complete response, PR = partial response, SD = stable disease; PD = progressive disease.

## Study Schema



## CD8 ImmunoPET: Correlation Between Baseline CD8 Uptake & Radiographic Response

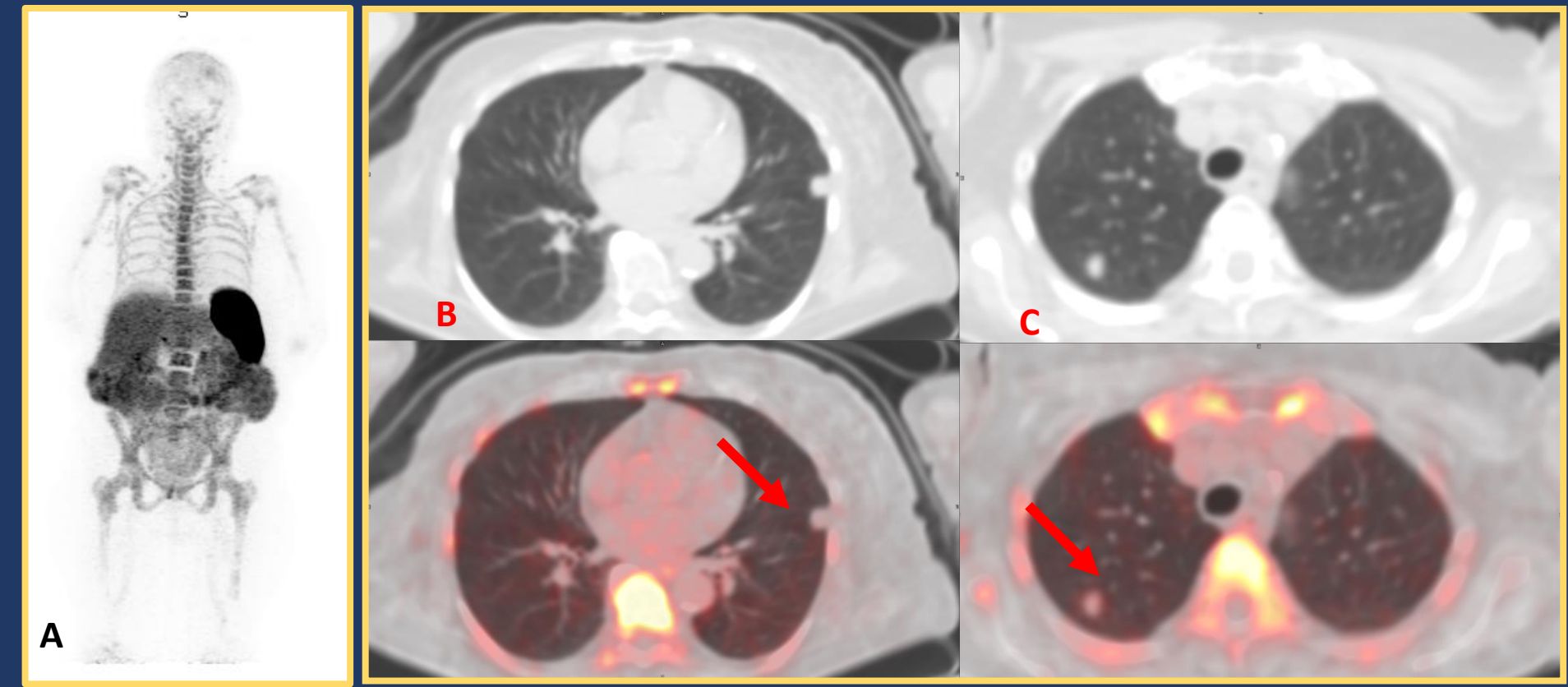
### Case Study 1: High CD8 Uptake & Complete Response



- The patient herein had clear cell mRCC with pulmonary metastases following left radical nephrectomy & right partial nephrectomy
- Nivolumab/ipilimumab started 5 days after the baseline scan
- Whole Body CD8 PET MIP (Fig A) reveals high CD8 uptake in multiple lymph nodes at baseline as well as moderate uptake in the largest lung lesion (B)
- The patient achieved a partial response (RECIST 1.1) at 89, 147 and 230 days and complete response at 314 days

Location	SUV <sub>max</sub> (peak)	Figure
Right Lung	3.62 (3.14)	B
Cervical LN	10.37 (7.11)	Not visualized
Supraclavicular LN	9.32 (6.57)	Not visualized
Axillar LN	12.69 (7.51)	B and C
Mediastinal LN	16.56 (10.28)	C
Retroperitoneal LN	19.95 (15.34)	Not visualized
Pelvic LN	10.83 (7.65)	D
Inguinal LN	17.00 (10.99)	Not visualized

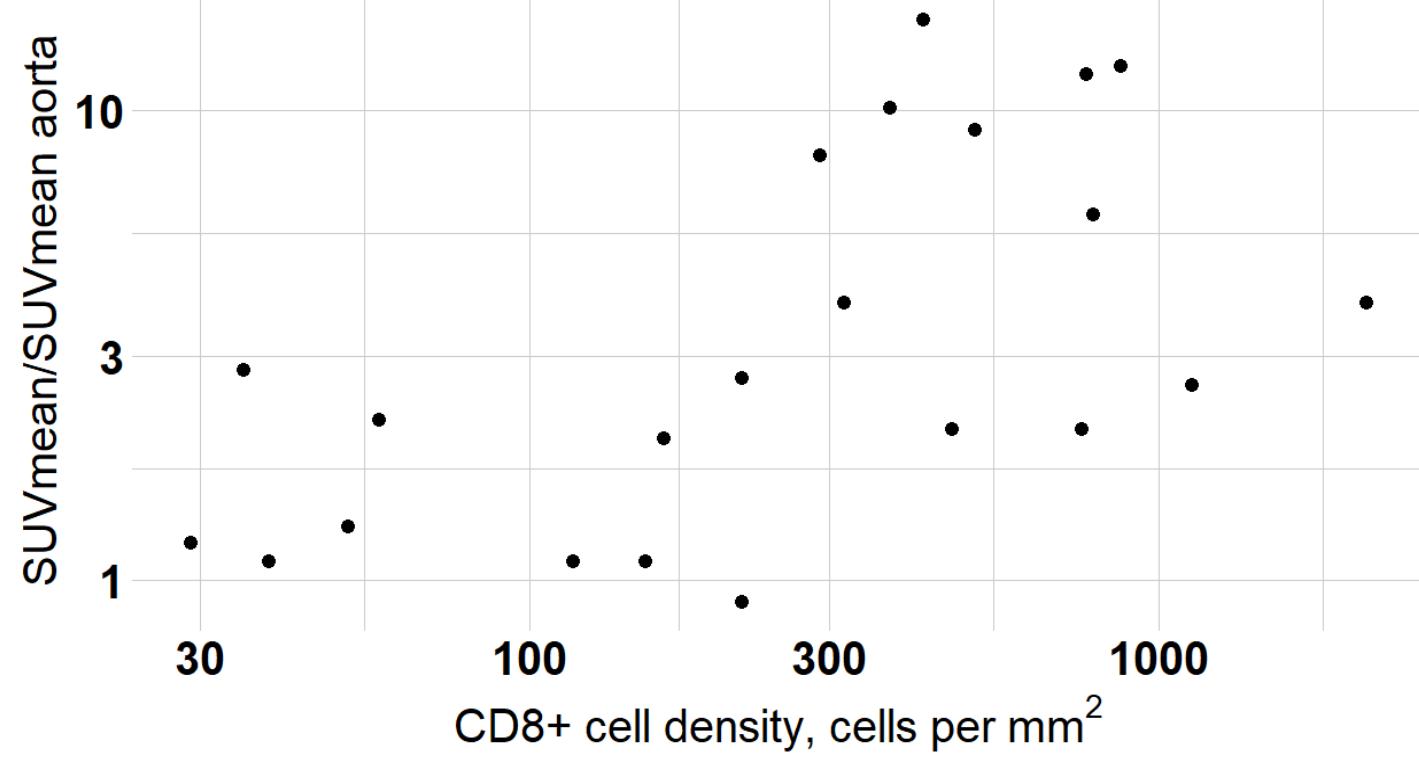
### Case Study 2: Low CD8 Uptake & Progressive Disease



- The patient herein had clear cell mRCC with pulmonary metastases following left radical nephrectomy
- Patient had previously received chemotherapy and radiotherapy for breast cancer
- Nivolumab/ipilimumab was initiated 2 days after the baseline scan
- Whole Body CD8 PET MIP (Fig A) reveals minimal CD8 uptake in cervical nodes at baseline read as negative
- Less pronounced CD8 uptake in the bone marrow compared to case study 1
- The SUV<sub>max</sub> (peak) of the left lung lesion (Fig B) is 1.38 (1.18) & of the right lung lesion (Fig C) is 1.58 (1.21)
- The patient showed stable disease at 84 days and progressive disease at 145 days and 229 days

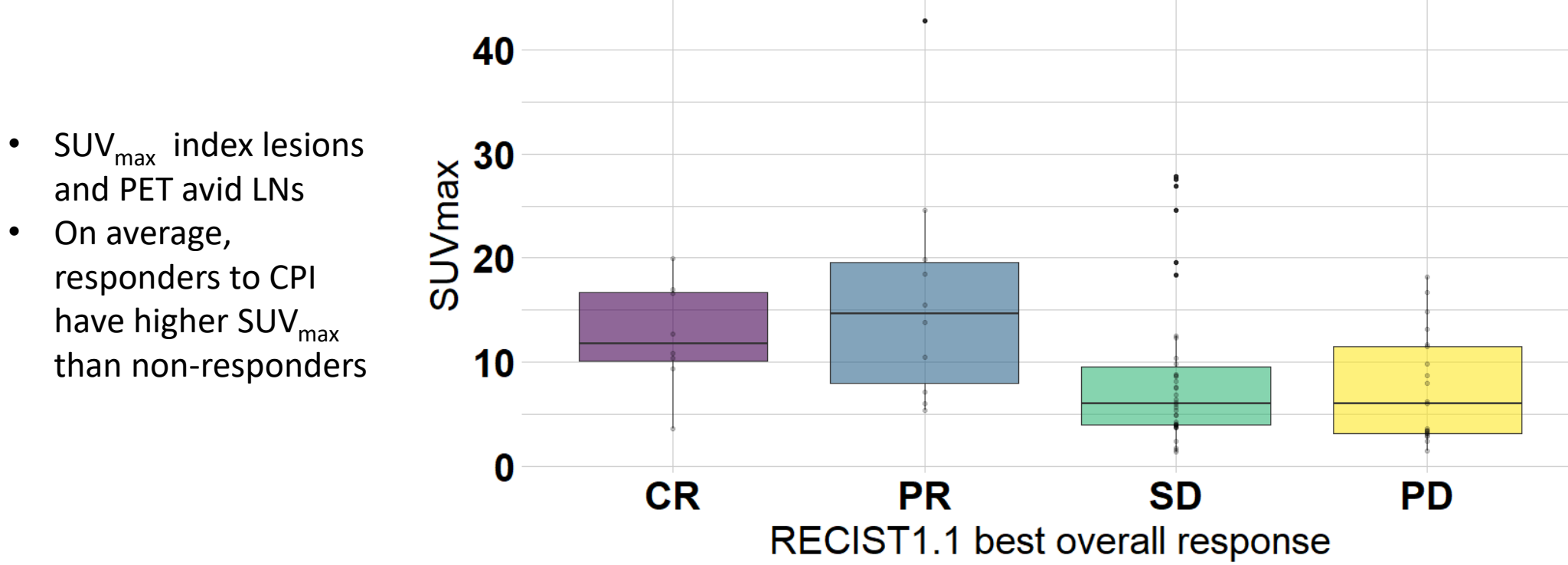
## Results

### Correlation of lesion SUVmean with CD8 cell density



- PET avidity and CD8+ cell expression were compared using the Spearman correlation coefficient
- Strong correlation observed, Spearman 0.72, p<0.0003, between SUV<sub>mean</sub> lesion/SUV aorta and the CD8+ cell density measured as CD8+ cells per mm<sup>2</sup>

### Baseline SUVmax - index lesions and PET avid LNs



- Average SUV<sub>max</sub>, SUV<sub>peak</sub> and SUV<sub>mean</sub> per patient among all quantified index lesions and representative lymph nodes were 9.74, 6.67 and 5.93 for baseline and 9.07, 6.44 and 5.54 during treatment, respectively
- Average SUV<sub>max</sub> at baseline was 14.68 in responders to CPI and 8.23 in non-responders (P<0.0008, Wilcoxon Signed-Rank Test). On treatment, SUV<sub>max</sub> was 10.86 in responders to CPI and 8.49 in non-responders (P=0.58, Wilcoxon Signed-Rank Test)

## Conclusions

- To our knowledge, this is the first series in patients with RCC to demonstrate that functional imaging of immune cells (in this case, CD8+ cells) may segregate response to CPIs, with responders having a higher baseline SUVmax and a larger decrement in SUV with therapy
- Early changes in lesion size in some pts indicate the on-treatment imaging timepoint may have been too late to see the peak CD8 T-cell density
- The contribution of the CD8+ LN to those findings will have to be evaluated in further studies
- Our results are bolstered by a significant correlation between tissue and imaging CD8 expression.
- Larger studies are underway to validate this noninvasive imaging strategy. (NCT05013099)