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

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**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 CheckMate 238 Trial (NCT03802123), a study assessing crefimirlimab (a 89 Zr-labeled minibody with high affinity for CD8) in patients receiving CPIs for advanced cancer.
- We hypothesize that functional imaging of CD8+ T-cells in mRCC 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 Nivolumab/ipilimumab.

**Study Schema**

**Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (range)</td>
<td>64 (54-71)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male: 8/7</td>
</tr>
<tr>
<td>Histology, N (%)</td>
<td>Papillary: 12/7, Clear cell: 4/5, Non-clear cell: 0/1</td>
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<tr>
<td>SUVmax of all contoured lesions in the CD8 PET was compared to the Best Overall Response (RECIST 1.1) using the Wilcoxon Signed Rank Test.</td>
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**Patient Characteristics**

**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.
- Neoadjuvant/ipilimumab started 5 days after the baseline scan.
- Whole Body CD8 PET MIP (Fig A) reveals high SUV max of the largest lung lesion (B).
- The patient achieved a partial response (RECIST 1.1) at 85, 147 and 230 days and complete response at 145 days.

**Case Study 2: Low CD8 Uptake & Progressive Disease**
- The patient herein had clear cell mRCC with pulmonary metastases following left radical nephrectomy & right partial nephrectomy.
- Neoadjuvant/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 patient achieved a partial response (RECIST 1.1) at 138, 118 & of the right lung lesion (Fig B) is 3.58 (2.21).
- The patient showed stable disease at 84 days and progressive disease at 145 days and 229 days.

**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 aggregate 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 promising imaging strategy. (NCT0513099)