Radiographic Predictors of Response to 177Lu-DOTATATE

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Background

- Can we identify early the gastroenteropancreatic neuroendocrine tumor (GEP-NET) patients most likely to benefit from 177Lu-DOTATATE, the newly approved peptide receptor radionuclide therapy (PRRT)?
- **Hypothesis:** pre-treatment maximum standardized uptake value (SUVmax) on DOTATATE scans and mid-treatment radiographic response predict overall response to 177Lu-DOTATATE.

Material & Methods

- We identified patients at University of California, San Francisco (UCSF) who received 177Lu-DOTATATE through the expanded access protocol (Table 1. N=18, median age 63 years, 44% male, 78% midgut).
- Open-label trial for patients with inoperable, well-differentiated NETs progressing despite somatostatin analog therapy (NCT02705313).
- Patients received up to 4 cycles of 177Lu-DOTATATE and underwent restaging CT or MRI scans mid-treatment after 2 cycles, immediately following completion of therapy (”post treatment”), and then per routine clinical follow-up (“last follow up”).
- We determined SUVmax for the 16 patients with baseline 68-Ga-DOTATATE/TOC PET scans.
- Objective response rate (ORR) determined via RECIST 1.1.
- Spearman non-parametric correlations were used to determine associations between continuous variables.

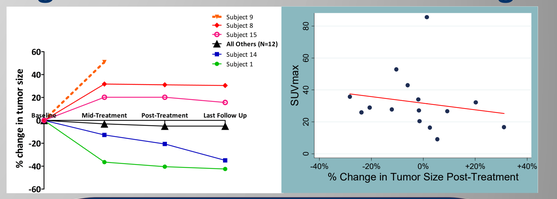
Table 1:
Study Population Characteristics

Characteristic	N=18
Median age (IQR)	63 (52-66)
Females, % (N)	10 (56%)
Primary Site, % (N)	
Small bowel	78% (14)
Pancreas	6% (1)
Bronchial	6% (1)
Renal	6% (1)
Unknown	6 % (1)
Grade, % (N)	
1	44% (8)
2	56% (10)
Median Ki-67%	2.9%
SUVmax, median (IQR)	28 (23-39)

Results

- We observed high baseline 68-Ga-DOTATATE/TOC uptake in this population, with a median SUVmax of 28 (interquartile range (IQR): 23-39).
- ORR immediately after therapy completion was low (6%), but most patients achieved stable disease (77%). A minority of patients progressed (17%; Figure 1).
- We found a strong association between the % change in tumor size on the mid-treatment scan after 2 cycles and the post treatment scan (Spearman rho 0.83, p <0.001).
- There was also a strong association between the % change in tumor size on the mid-treatment scan and last follow up scan (rho 0.92, p<0.001).
- Patients with higher baseline SUVmax tended to have more disease shrinkage on the post treatment scan, although this was not statistically significantly (rho -0.41, p=0.13; Figure 2).

Figure 1 and 2: Click Here to Enlarge



Conclusions

- Both disease progression and response to PRRT tended to occur early, by mid treatment scan after first 2 cycles.
- Further investigation in larger, prospective studies is merited to confirm whether baseline SUVmax predicts treatment response to PRRT.
- Importance of defining rate of disease progression pre-treatment.
- Study limitations: heterogeneity of imaging modalities, small sample size, limited follow up.
- Hypothesis generating regarding patient selection and when to stop PRRT.

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Results, Continued

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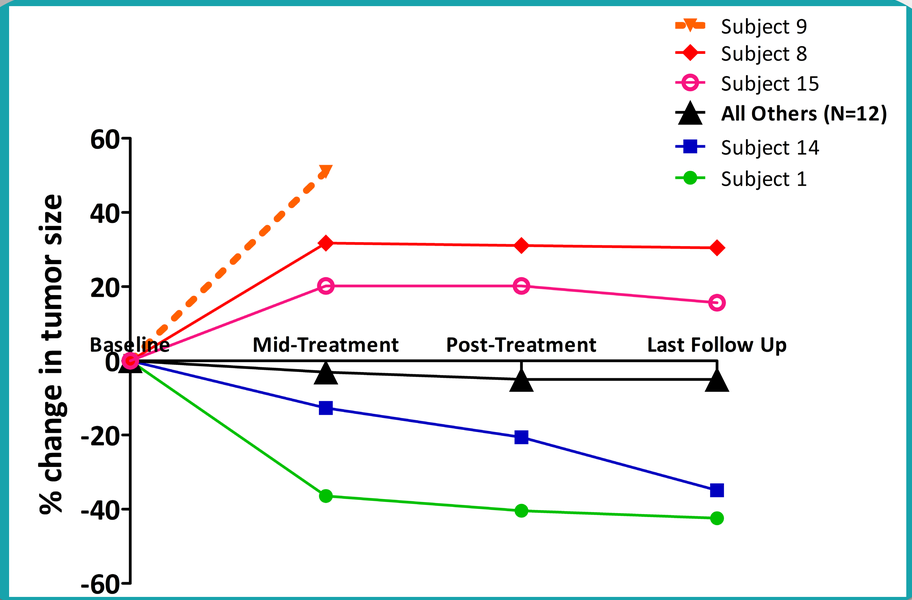
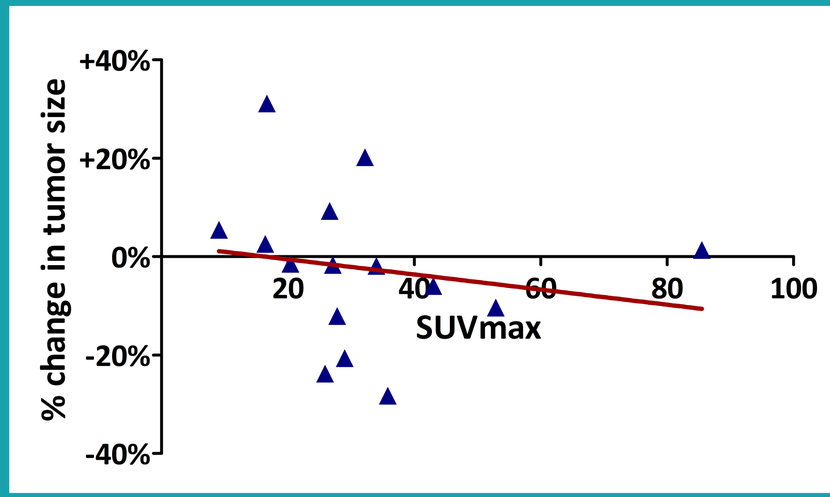
Figure 1. % Change in Target Lesion Size with Treatment for Patients with Progressive Disease Compared to Those with Stable Disease or Partial Response



- Individual patient-level response data are shown for the patients (N=3) with progressive disease (Subjects 9, 8, and 15), along with the patients (N=2) who achieved an objective response by last follow up (Subject 1, 14).
- Subject 9 died from rapidly progressive disease shortly after completing 2 cycles of therapy. Subjects 8 and 15 progressed on their mid-treatment scans, but subsequently had a period of disease stability in the absence of additional therapies.
- In contrast, the other (N=12) patients on this study had generally stable disease; mean % change in tumor size at each timepoint is depicted in the figure above.
- **Click here to see radiology images for example patients**

Figure 2. Scatterplot of Baseline SUVmax and % Change in Tumor Size following PRRT



- Patients with higher baseline pre-treatment SUVmax tended to have more disease shrinkage on their post-treatment scans, although this was not statistically significantly (rho -0.41, p=0.13).
- This association is even stronger if the one SUV outlier is excluded (rho -0.50, p=0.066).
- We found a similar association between SUVmax and % change in tumor size on last follow up scan (rho -0.51, p=0.090).
- Further investigation in larger, prospective studies is warranted to confirm whether baseline SUVmax predicts treatment response.

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Results, Continued

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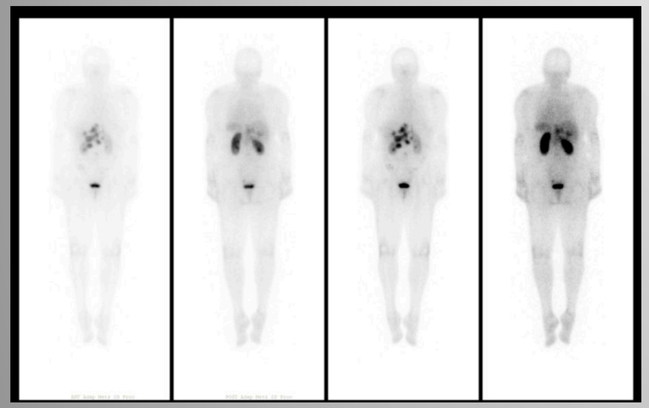
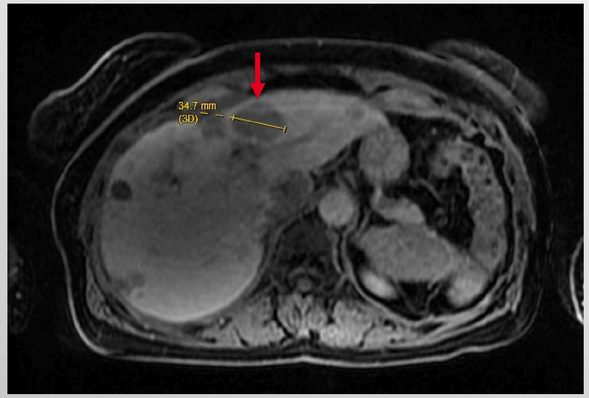
Figure 3. Scans for Subject with Partial Response

A. Pre-Treatment OctreoScan MIP 2.9.2017



B. Pre-Treatment MRI Liver (2.17.2017)



C. Post-Treatment MRI Liver (5.4.2018) Last Follow Up

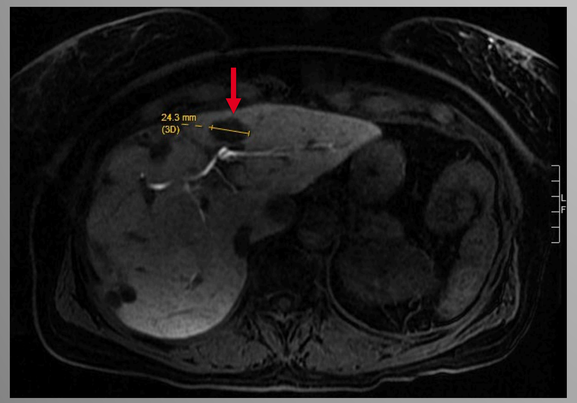
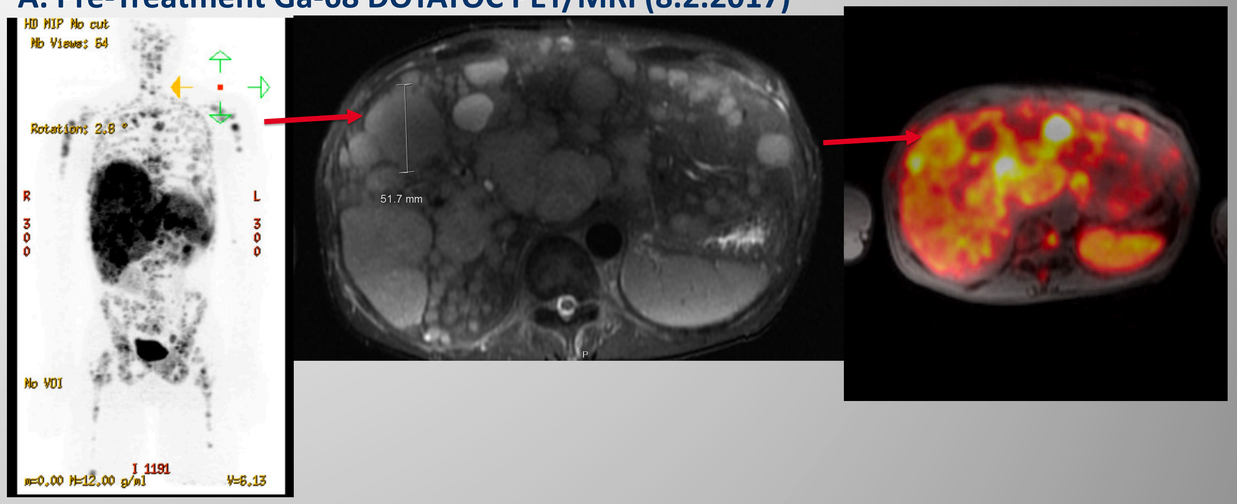
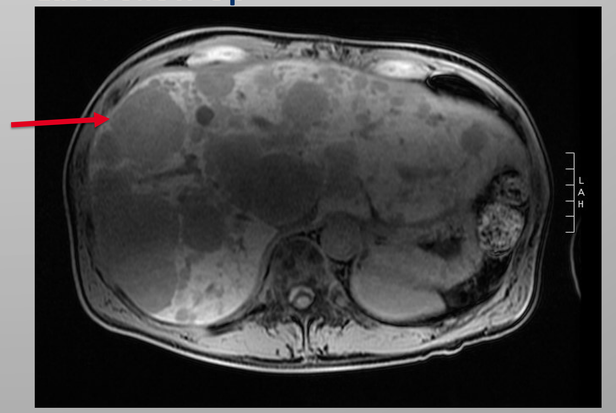


Figure 4. Scans for Subject with Stable Disease

A. Pre-Treatment Ga-68 DOTATOC PET/MRI (8.2.2017)



B. Post-Treatment MRI Liver (5.16.2018) Last Follow Up



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