Abstract 37

Quantitative assessment of PSMA imaging before and after ^{177}Lu-PSMA-617 treatment in a Ph I/II trial

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Background

Prostate Specific Membrane Antigen targeted radiotherapy (**PSMA-TRT**) allows exquisite delivery of ionizing radiation

A single dose-intense cycle of **^{177}Lu-PSMA-617** is effective in pretreated mCRPC w/o requiring PSMA+ PET to enroll[1]

Prior *post hoc* analyses of the most PSMA-positive disease sites have demonstrated **associations of PSA response and PFS with ^{68}Ga-PSMA11-PET signal**

Methods

13 subjects from our ph I/II trial of fractionated-dose (D1, D15) 177Lu-PSMA-617[2] were analyzed via TRAQinform IQ technology (AIQ Solutions), providing PSMA signal:

- pre- and post-treatment in lesions
- changes for individual lesions[3]
- pre- and post-treatment in healthy tissues & salivary glands

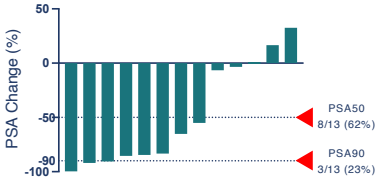
Test/re-test imaging within 6-72 hr was used (n=3) to determine limits of agreement in scan-to-scan variation

Extracted measures include SUVmax, SUVmean, SUVtotal (TLG-equivalent), Active PET Volume, and SUVhetero (heterogeneity within the lesion)[4]

Trial Summary

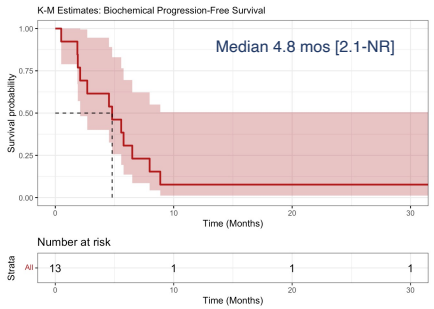
Baseline Demographics (n=13)	
Age, median (range)	68 (56-77)
PSA, median (range)	179.6 (4.93-923.3)
CALGB (Halabi) Prognostic Group	
Low	0 (0)
Intermediate	2 (15)
High	11 (85)
Sites of Metastasis, n (%)	
Bone	13 (100)
Lymph Node	10 (77)
Lung	5 (38)
Liver	3 (23)
Prior Therapy, n (%)	
2+ potent AR inhibitors	4 (31)
Chemotherapy	6 (46)
Radium-223	3 (23)
Sipuleucel-T	5 (39)
PSMA-TRT	0 (0)

Treatment Emergent AEs, n (%)			
	Gr 1	Gr 2	Gr 3/4
Xerostomia	9 (69)	1 (8)	0 (0)
Nausea	8 (62)	0 (0)	0 (0)
Pain	3 (23)	3 (23)	0 (0)
Fatigue	10 (77)	0 (0)	0 (0)
Anemia	4 (31)	0 (0)	0 (0)
Transaminitis	1 (8)	0 (0)	0 (0)
Thrombocytopenia	2 (15)	0 (0)	0 (0)
Neutropenia	2 (15)	1 (8)	0 (0)



Results

Improved biochemical PFS: Associated with pretreatment SUV_{mean}

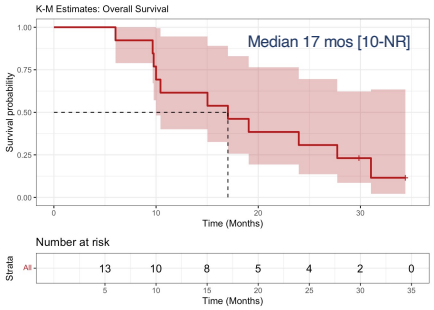


Characteristic	N	HR[1]	95% CI[1]	p-value
Delta SUV Heterogeneity	13	1.00	0.99, 1.01	0.50
Delta SUV Max	13	1.01	1.00, 1.02	0.28
Delta SUV Mean	13	1.01	0.99, 1.04	0.19
Delta SUV Total	13	1.00	1.00, 1.01	0.088
Delta Volume	13	1.01	1.00, 1.02	0.011
Pre SUV Heterogeneity	13	0.95	0.89, 1.00	0.057
Pre SUV Max	13	0.99	0.97, 1.00	0.094
Pre SUV Mean	13	0.66	0.49, 0.90	0.009
Pre SUV Total	13	1.00	1.00, 1.00	0.27
Pre Volume	13	1.00	1.00, 1.00	0.93

[1] HR = Hazard Ratio, CI = Confidence Interval

- Pretreatment PSMA (SUV_{mean}) predicts biochemical PFS
- A trend toward longer PFS was associated with change in PSMA+ tumor volume

Longer OS: Associated with pretreatment SUV_{mean}



Characteristic	N	HR[1]	95% CI[1]	p-value
Delta SUV Heterogeneity	13	1.00	0.99, 1.01	0.42
Delta SUV Max	13	1.01	1.00, 1.02	0.25
Delta SUV Mean	13	1.02	0.99, 1.05	0.13
Delta SUV Total	13	1.00	1.00, 1.01	0.19
Delta Volume	13	1.01	1.00, 1.01	0.057
Pre SUV Heterogeneity	13	0.97	0.92, 1.02	0.18
Pre SUV Max	13	0.99	0.98, 1.01	0.39
Pre SUV Mean	13	0.81	0.65, 1.00	0.048
Pre SUV Total	13	1.00	1.00, 1.00	0.64
Pre Volume	13	1.00	1.00, 1.00	0.13

[1] HR = Hazard Ratio, CI = Confidence Interval

- Pretreatment PSMA (SUV_{mean}) predicts longer OS (HR 0.66, 95% CI 0.49-0.90, p = 0.009)
- A trend toward longer OS was associated with change in PSMA+ tumor volume

Pretreatment PSMA PET SUVs predict AEs

Higher pretreatment salivary gland SUV_{max} was associated with development of xerostomia

No xerostomia (n=3): 17.4 [16.8, 22.4]
Xerostomia (n=10) : 26.1 [20.2, 30.7]
median [IQR], p = 0.4

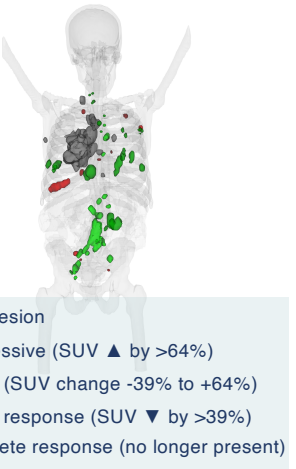
Bony pain flare was more common in subjects with *lower* pretreatment PSMA scores in *unaffected* regions of skeleton

SUV_{total}

Without pain (n=7): 3062 [2715, 3655]
With pain (n=6): 2348 [2130, 2578] (median, IQR), p = 0.051

TRAQinform IQ Representative Image

Automatically detects and matches lesions across time points



Conclusions

Using AI-based quantification of PSMA expression on pre- and post-treatment ^{68}Ga-PSMA11-PETs, we observe:

1. Associations between PSMA PET SUV and response by both **overall survival (OS)** and **PSA response**
2. Associations between degree of PSMA PET SUV in **PSMA-expressing non-tumor tissues and adverse events** (AEs)

Expansion and refinement of this algorithm may improve our ability to **anticipate toxicity** by body-wide PSMA detection and **predict treatment response**

Contact Information

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Support & Citations

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