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**14. ABSTRACT**

Prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy (TRT) builds upon the radiosensitivity of prostate cancer with the specific expression of PSMA. We hypothesize that there are patient (germline) and/or tumor molecular characteristics such as DNA repair defects and active AR signaling as well as clinical characteristics that are associated with response (or lack thereof) to PSMA-TRT. We hypothesize that quantitative molecular imaging assessment of PSMA expression will be associated with response to PSMA-TRT. We also hypothesize that PSMA-TRT generates an immune response that may be identified and associated with patient outcome. In this proposal, we will utilize our retrospective and prospective data and sample sets to: (i) assess genomic biomarkers and gene expression changes associated with outcome from anti-PSMA targeted radionuclide therapy; (ii) assess clinical parameters associated with outcome from anti-PSMA- TRT; (iii) assess PSMA expression as determined by PSMA molecular imaging associated with response to anti-PSMA –TRT; and (iv) evaluate generation of an immune response following anti-PSMA-TRT in association with clinical outcome.

This project addresses the overarching challenge to develop effective new treatments and address mechanisms of resistance and particularly addresses the Focus Areas of Imaging and Targeted Radionuclide Therapy and Therapy and Mechanisms of Resistance and Response. As it is clear that prostate cancer is a radiosensitive disease, and PSMA is highly and selectively expressed, but not all patients respond to PSMA TRT, this proposal will rapidly translate into clinical progress for men afflicted with advanced prostate cancer in the near term. Furthermore, such targeted therapy may lead to future cures for men with micrometastatic disease in the high-risk clinically localized or biochemically recurrent settings.

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## 1. INTRODUCTION:

Prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy (TRT) is a promising new class of drugs for men with metastatic prostate cancer. PSMA is an ideal target because its expression is highly specific for prostate cancer, it is expressed by the vast majority of hormone naïve and castration resistant tumors, and its cell surface expression lends opportunities for both imaging and therapy. Based on promising data led by our team and others looking at PSMA radionuclide therapy, $^{177}$Lu--PSMA-617 is now completing a phase 3 trial for men with castration resistant prostate cancer. While the field is excited and encouraged by anti-tumor activity, there is still much to learn about patient and/or tumor molecular characteristics associated with response (or lack thereof) to PSMA-TRT. In this study, we are evaluating genomic biomarkers, clinical features, and PSMA molecular imaging of prospective cohorts of men treated with PSMA radionuclide therapy on our clinical trials.

## 2. KEYWORDS:

Prostate cancer specific membrane antigen (PSMA), metastatic prostate cancer, radionuclide therapy, biomarkers, genomics

## 3. ACCOMPLISHMENTS:

**What were the major goals of the project?**

Our goal is to define molecular biomarkers and clinical features associated with outcomes from anti-PSMA targeted radionuclide therapy. We are performing prospective and retrospective genomic analyses of archival tissues, plasma samples, and metastatic biopsies from patients treated on prospective anti-PSMA targeted radionuclide clinical trials, with correlation of genomics with outcomes including PSA and radiographic response, progression free survival (PFS), and overall survival. We are also correlating genomics with PSMA PET/CT imaging to evaluate genomic characteristics associated with PSMA low or PSMA-heterogeneous disease and resistance to PSMA radionuclide therapy. PSMA expression and other imaging parameters are being quantified and correlated with response and outcomes. Immune responses following anti-PSMA targeted radionuclide therapy are also being measured, including an assay to measure serologic immunoreactivity to a targeted panel of antigens before/after PSMA-TRT. Overall this project will provide unprecedented insights into the molecular mediators of response and resistance to PSMA targeted radionuclide therapies with broad implications for the field.

**What was accomplished under these goals?**

We have made the following progress on our Aims according to our SOW:

Aim 1: To prospectively and retrospectively assess genomic biomarkers associated with outcome from anti-PSMA targeted radionuclide therapy

Major Task 1-1: Characterize genomic landscape of prior patients with mCRPC treated with PSMA-TRT [Tagawa and Beltran]

In the initial portion of this Aim, we analyzed clinically available genomic alterations in our retrospective dataset. The subset analyzed with whole exome sequencing (WES) and the larger dataset analyzed across CLIA-approved next generation sequencing platforms were reported in presentations at major scientific conferences in 2019 as described in Products.

We have completed subtask 1 for this Aim.

Subtask 2 has been completed, with extraction of DNA occurring in 2021.

Subtask 3 has been completed, with results of tissue genomic correlates with trial outcomes presented at the 2020 AACR Scientific Meeting.

Major Task 1-2: Characterize genomic landscape of prospective patients with mCRPC treated with PSMA-TRT [Tagawa and Beltran]

Subtask 1 is completed.

Subtask 2 is partially complete and will be completed; all baseline specimens have been collected and processed. Follow up specimens will be processed once follow up on the associated therapeutic clinical trials is completed.

Subtask 3 has been completed on baseline specimens; processing of post-treatment specimens will be completed with alternative funding once follow up on the associated therapeutic clinical trials is completed (after subtasks 1 and 2 completed for follow up specimens).

Subtask 4 is partially completed. Analysis of baseline data was performed in early 2022 with data publicly presented at the 2022 ESMO Scientific Meeting.

Progress to date: Because of the DNA damaging effects of ionizing radiation and of the relationship between the AR pathway and PSMA expression, we hypothesized that patients with germline or somatic gene alterations in DNA damage repair (DDR) pathways or DDR crosstalk pathways (AR, MYC) treated with PSMA-TRT may demonstrate differential treatment responses and outcomes. **Methods:** We examined a cohort of advanced PC patients with available germline (targeted) or/and somatic (targeted or whole exome) DNA testing, and clinical data (Halabi CALGB prognostic factors) and outcome. The Kaplan-Meier method and Cox regression analysis were used to evaluate the associations between mutations/copy number alterations (CNA) with PSA response (≥50%, ≥30%, any) and radiographic response, progression-free survival (PFS) and overall survival (OS). Stepwise forward-selection method was used in the multivariable regression model and p value for entry was set at 0.1. For final analyses, a $p \leq 0.05$ was used for statistical significance. We analyzed 53 patients treated with

PSMA-TRT. 16 (30.2%) received $^{177}$Lu-J591, 28 (56.6%) $^{177}$Lu-PSMA-617, 4 (7.5%) both concurrently, 2 (3.8%) received $^{225}$Ac-J591 (3 additional received more than 1 agent sequentially and are analyzed based upon 1st drug). 6 (11.3%) had pathogenic germline DDR mutations while 31 (58.5%) had ≥1 mutation/CNA in DDR genes. The most frequently affected DDR genes were: TP53 (n=21, 39.6%), BRCA2 (n=14, 26.4%), CHEK2 (n=10, 18.9%), FANCA (n=10, 18.9%), RB1 (n=9, 16.9%), ATM (n=5, 9.4%), ERCC5 (n=5, 9.4%), ERCC3 (n=3, 5.7%), ERCC2 (n=2, 3.8%), BRCA1(n=2, 3.8%), MSH6 (n=2, 3.8%), FANCD2 (n=2, 3.8%), FANCF (n=2, 3.8%). AR amplifications or resistance-mutations were found in 22 patients (41.5%), and MYC amplifications in 9 patients (16.9%). 19 (35.8%) patients had ≥50% PSA decline, 24 (45.3%) experienced ≥30% decline and 39 (73.6%) had any PSA decline following PSMA-TRT. 4 patients experienced a partial response while 18 had stable disease. Presence of BRCA2 inactivating mutations, deletions or losses was associated with any PSA decline (p=0.011). PFS was significantly longer in patients with RB1 deletion or loss (5 vs 3 mos, p=0.003). The presence of BRCA2 alterations was predictive of longer OS compared to wild-type patients (49 vs 17 mos, p=0.09). AR amplifications or resistance-mutations and MYC amplifications were both predictive of shorter OS (AR: 13 vs 63 mos, p=0.02; MYC: 8 vs 24 mos, p=0.06). On multivariate analysis, after adjusting for Halabi prognostic groups (low vs high risk), BRCA2 and AR alterations retained their significance as independent prognosticators of OS (BRCA2 HR 0.1 [0.02-0.42], p=0.002; AR HR 7.2 [2.09-25.14], p=0.002).

We have recently extracted DNA and performed targeted sequencing via the PCF SELECT platform utilizing pre-treatment plasma specimens obtained from the initial subset of patients enrolled in clinical trials. In addition, a larger number of archival tissue specimens from more recently enrolled/treated clinical trial subjects has been processed, with targeted genomic sequencing performed via the Oncomine platform. A similar analysis as above will be conducted using the clinical information.

**Conclusions:** Knowledge of molecular alterations in BRCA2, AR and RB1 genes may have potential utility for prediction of clinical outcomes in patients being considered for anti-PSMA targeted radionuclide therapies. We are expanding on these finding in larger and prospective cohorts as described above.

<u>Aim 2: To prospectively and retrospectively assess clinical parameters associated with outcome from anti-PSMA targeted radionuclide therapy</u>.

Major Task 2-1: Associate clinical characteristics of patients with mCRPC with outcome from PSMA-TRT [Tagawa and Beltran]

Subtask 1 is complete.

Subtask 2 is complete.

Subtask 3 is complete and has been reported at international meetings (ESMO, ASCO).

Progress: We initially evaluated 46 pts treated with PSMA targeted therapies between 2007-2018 after progression on at least two therapeutic lines, including abiraterone or enzalutamide (76.1%). 28 (60.9%) pts

were Halabi high-risk group. PSA decline by at least 50% was observed in 34.8%, median PFS was 5.77 months (95% CI 4.33-7.28), and median OS was 19.15 months (95% CI 12.23-51.25). WES data (n=28) showed an incidence of *AR, BRCA1, BRCA2, ATM* alterations (copy number variations and point somatic mutations) in 71.4% (n=20), 11.1% (n=3), 29.6% (n=8), and 14.3% (n=4), respectively. Variables found with backward selection with AIC criterion for PFS and OS suggest significant clinical and molecular predictors of PFS/OS (Table 1).

**Table 1. Predictors of PFS and OS in advanced prostate cancer patients treated with PSMA targeted therapy**

| **Backward stepwise selection for PFS** | | | **Backward stepwise selection for OS** | | |
|---|---|---|---|---|---|
| **Variable** | **HR (95% CI)** | **P** | **Variable** | **HR (95% CI)** | **P** |
| Previous abi/enza | 2.75 (0.93,8.08) | 0.067 | Previous abi/enza | 6.78 (1.17,39.21) | 0.032 |
| Baseline LDH | 1.01 (1.00,1.02) | 0.003 | Baseline ALP | 1.02 (1.01,1.04) | <0.001 |
| BRCA1 alteration | 0.05 (0.01,0.53) | 0.012 | BRCA2 alteration | 0.07 (0.01,0.53) | 0.010 |
| BRCA2 alteration | 0.26 (0.09,0.76) | 0.014 | AR alteration | 8.38 (1.26,55.84) | 0.028 |

In analysis of 80 patients with plasma and PBMCs collected prospectively prior to PSMA-TRT, high allele-specific ploidy (asP analyzed as diploid vs high) was associated with lower likelihood of response (OR 0.48, 95% CI 0.16-1.47, p=0.20) and poorer overall survival (HR 2.14, 95% CI 1.15-4, p=0.017). AR copy number gain was associated with fewer PSA responses (OR 0.47, 95% CI 0.14-1.49, p=0.20) and poorer overall survival (HR 2.69, 95% CI 1.40-5.18, p=0.003).

**Conclusion:** Knowledge of previous therapy with AR-directed drugs, baseline LDH, ALP, and *AR* and *BRCA1/BRCA2* alterations may have potential clinical utility in patients being considered for anti-PSMA therapies. Utilizing ctDNA analysis, a non-invasive technique, in patients undergoing PSMA-TRT demonstrate that AR copy number gain and high allele-specific ploidy, reflecting genomic instability and complex karyotype, are associated with poorer prognosis.

Aim 3: To prospectively and retrospectively assess PSMA expression as determined by PSMA molecular imaging associated with response to anti-PSMA targeted radionuclide therapy

Major Task 3-1: Associate clinical characteristics of prior patients with mCRPC with outcome from PSMA-TRT [Tagawa and Bander]

Subtask 1 is complete and has been reported in a presentation at a major scientific conference in 2019 and published in a peer reviewed journal as described Products below.
Subtask 2 is complete and has been reported as described below.
Progress: We analyzed images and clinical outcome from 215 men receiving PSMA-TRT. Higher PSMA expression as determined by PSMA imaging was associated with a higher likelihood of response to treatment (p=0.006) on univariate analysis. On multivariable analysis, stronger PSMA imaging remained associated with response even after controlling for clinical prognostic factors, radioactive dose administered, and prior chemotherapy (p=0.006). However, a small subset with no or limited PSMA expression as determined by imaging had PSA response. These data were initially presented in 2019 and published in 2021.
Preliminary analysis of pre-treatment PSMA imaging has been performed on the individual trials as presented at ASCO 2021 (for 225Ac-J591 and ESMO 2021 (for 177Lu-PSMA-617). A combined analysis was presented at the 2021 Society of Urologic Oncology annual meeting.
**Conclusion:** These data support the hypothesis that high PSMA uptake on imaging is associated with response to PSMA-TRT, but there are a small subset with poor pre-treatment imaging that may respond to PSMA-TRT.

Aim 4: To evaluate generation of an immune response following anti-PSMA targeted radionuclide therapy in association with clinical outcome
Major Task 4-1: To assay serologic immunoreactivity to a targeted panel of antigens before/after PSMA-TRT and associate with outcome [Tagawa and Bander]
Collection of specimens for subtasks 1 and 2 is complete.
Analysis is underway and will be finalized once follow up to the associated therapeutic clinical trials is completed.

Major Task 4-2: To assay serologic immunoreactivity against a broad array of antigens before/after PSMA-TRT and associate with outcome. [Tagawa and Bander]
Subtask 1 was attempted, but unsuccessful due to loss/damage of old serum.
Collection of specimens for subtask 2 is complete.
Analysis will be completed once follow up to the associated therapeutic clinical trials is completed.

Major Task 4-3: To assess immunogenic cell death following PSMA-TRT
Subtask 1 was attempted, but unsuccessful due to loss/damage of old serum. [Tagawa and Bander]
Collection of specimens for subtasks 2 and 3 is complete.
Analysis will be completed once follow up on the associated therapeutic clinical trials is completed.

**What opportunities for training and professional development has the project provided?**

Trainees and fellows in our groups participate and lead analyses related to this study. Through meetings and interactions between scientific and clinical investigators, trainees and fellows are provided unique learning opportunities in translational research. Dr. Conteduca and Dr. Vlachostergios were first authors and presented abstracts on findings from this study at GU ASCO, AACR, and ASCO in 2019 and were co-authors of abstracts presented in 2020. Dr. Vlachostergios is first-author of manuscripts on PSMA imaging and response to PSMA-TRT as well as PSMA imaging and prognosis in mCRPC which were published in 2021. Dr. Sun was first author on the presentation of archival tissue analysis and prospective plasma ctDNA results as associated with outcomes from PSMA-TRT at the 2020 AACR and 2022 ESMO annual scientific meetings.

**How were the results disseminated to communities of interest?**

Results were presented as meeting abstracts at national/international meetings in 2019, 2020, 2021, 2022 and 2023 (GU ASCO, AACR, ASCO, and ESMO) and have been published in peer-reviewed literature (see Products section below). We have also participated in meetings, seminars, and interviews to disseminate results including through the Prostate Cancer Foundation and UroToday.

**What do you plan to do during the next reporting period to accomplish the goals?**

Analysis of the final samples is ongoing while clinical trial follow up is being completed. We plan to present new findings at. national / international meetings and to publish results. Dr. Beltran's Laboratory has recently hired a highly qualified lab manager, computational biologist and research technician to help conduct the remaining work in this proposal.

## 4. IMPACT:

**What was the impact on the development of the principal discipline(s) of the project?**

PSMA targeted radionuclide therapy is a new drug approach for men with metastatic castration resistant prostate cancer, which received FDA-approval in 2022. This study is providing new insights into molecular mediators of response and resistance to PSMA targeted radionuclide therapy, which may help in the future to select the patients most likely to benefit and to inform the development of effective combination strategies to prevent or target resistance mechanisms. The genomic analyses and correlation with imaging and immune markers will also provide new knowledge on tumor heterogeneity and how host responses impact therapy response and progression.

**What was the impact on other disciplines?**

Results from this project may provide insights into biomarker of response /resistance to radionuclide targeted therapies in other tumor types.

**What was the impact on technology transfer?**

Nothing to report

**What was the impact on society beyond science and technology?**

Nothing to report

## 5. CHANGES/PROBLEMS:

**Changes in approach and reasons for change:**

Nothing to report

**Actual or anticipated problems or delays and actions or plans to resolve them**

Commented [STT1]: This is the section that may need to be updated based upon DFCI NCE letter

Due to multiple communication issues, HRPO approval was delayed (initial communication was that a separate protocol was not necessary). This has now been resolved.
Two subaims involved previously collected and frozen serum from subjects enrolled in prior clinical trials. This serum was unfortunately lost and those subaims will not be able to be performed.
We had planned to extract DNA and perform targeted sequencing of samples in spring, 2020. However that was delayed due to the COVID-19 pandemic. We are completing in initial batches of these studies in late 2021.
We had planned to analyze serum samples for immunologic assays in spring, 2020. However that was delayed due to the COVID-19 pandemic. Final analysis of baseline samples was performed early 2022. Analysis of follow up samples is ongoing.
There have been delays in the continuity of research primarily due to delays in coordinating blood/tissues and DNA/RNA sequencing for the proposed correlative analyses and interruptions in hiring. However, Dr. Beltran's laboratory is operational and has recently hired a computational biologist who will be instrumental in conducting the remaining statistical analyses.

**Changes that had a significant impact on expenditures**

Nothing to report

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

The clinical trials associated with these studies have been affected by the COVID-19 pandemic. We anticipated completion of enrollment in the first half of 2020, but enrollment to the clinical trials was delayed by the pandemic. We completed enrollment in early 2021 and final subjects are in follow up.

**Significant changes in use or care of vertebrate animals**

Not applicable

**Significant changes in use of biohazards and/or select agents**

Not applicable

## 6. PRODUCTS:

**Journal publications.**

Miyahira AK, Pienta KJ, Morris MJ, Bander NH, Baum RP, Fendler WP, Goeckeler W, Gorin MA, Hennekes H, Pomper MG, Sartor O, Tagawa ST, Williams S, Soule HR. Meeting report from the Prostate Cancer Foundation PSMA-directed radionuclide scientific working group. Prostate. 2018 Aug;78(11):775-789. doi: 10.1002/pros.23642. Epub 2018 May 1. PMID: 29717499.

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Vlachostergios PJ, Niaz MJ, Sun M, Mosallaie SA, Thomas C, Christos PJ, Osborne JR, Molina AM, Nanus DM, Bander NH, Tagawa ST. Prostate-Specific Membrane Antigen Uptake and Survival in Metastatic Castration-Resistant Prostate Cancer. Front Oncol. 2021 Feb 18;11:630589. doi: 10.3389/fonc.2021.630589. PMID: 33680970; PMCID: PMC7930491.

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Osborne JR, Bander NH, Tagawa ST. Prostate-Specific Membrane Antigen Positron Emission Tomography and the New Algorithm for Patients With Prostate Cancer Prior to Prostatectomy. JAMA Oncol. 2021 Nov 1;7(11):1642-1643. doi: 10.1001/jamaoncol.2021.3762.PMID: 34529003.

Orlando F, Romanel A, Trujillo B, Sigouros M, Wetterskog D, Quaini O, Leone G, Xiang JZ, Wingate A, Tagawa S, Jayaram A, Linch M; PEACE Consortium; Jamal-Hanjani M, Swanton C, Rubin MA, Wyatt AW, Beltran H, Attard G, Demichelis F. Allele-informed copy number evaluation of plasma DNA samples from metastatic prostate cancer patients: the PCF_SELECT consortium assay. NAR Cancer. 2022 May 27;4(2):zcac016. doi: 10.1093/narcan/zcac016. PMID: 35664542; PMCID: PMC9154344.

Martinez J, Subramanian K, Castellanos SH, Thomas C, Choudhury AR, Muench B, Tagawa ST, Pillarsetty NVK, Osborne JR. Cyclotron vs generator-produced 68Ga PSMA: a single-institution, prospective clinical trial. Transl Oncol. 2023 Feb;28:101593. doi: 10.1016/j.tranon.2022.101593. Epub 2022 Dec 24. PMID: 36571987; PMCID: PMC9803810.

Stangl-Kremser J, Ricaurte-Fajardo A, Subramanian K, Osborne JR, Sun M, Tagawa ST, Bander NH. Response to RL-225Ac in prostate cancer: Effect of prior treatment with RL-177Lu: A systematic review of the literature. Prostate. 2023 Jul;83(10):901-911. doi: 10.1002/pros.24531. Epub 2023 Apr 13. PMID: 36960580.

Stangl-Kremser J, Sun M, Ho B, Thomas J, Nauseef JT, Osborne JR, Molina A, Sternberg CN, Nanus DM, Bander NH, Tagawa S. Prognostic value of neutrophil-to-lymphocyte ratio in patients with metastatic castration-resistant prostate cancer receiving prostate-specific membrane antigen targeted radionuclide therapy. Prostate. 2023 Oct;83(14):1351-1357. doi: 10.1002/pros.24597. Epub 2023 Jul 9. PMID: 37424145.

Tagawa ST, Thomas C, Sartor AO, Sun M, Stangl-Kremser J, Bissassar M, Vallabhajosula S, Huicochea Castellanos S, Nauseef JT, Sternberg CN, Molina A, Ballman K, Nanus DM, Osborne JR, Bander NH. Prostate-Specific Membrane Antigen-Targeting Alpha Emitter via Antibody Delivery for Metastatic Castration-Resistant Prostate Cancer: A Phase I Dose-Escalation Study of 225Ac-J591. J Clin Oncol. 2023 Nov 3:JCO2300573. doi: 10.1200/JCO.23.00573. Epub ahead of print. PMID: 37922438.

**Books or other non-periodical, one-time publications.** Nothing to report

**Other publications, conference papers and presentations**.

Vincenza Conteduca, Clara Oromendia, Panagiotis J. Vlachostergios, Amy Hackett, Charlene Thomas, Aidan Case, Jyothi Manohar, Kenneth Eng, Andrea Sboner, Karla V. Ballman, Olivier Elemento, David M. Nanus, Himisha Beltran, Scott T. Tagawa. Clinical and molecular analysis of patients treated with prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy. Presented at the 2019 Genitourinary Cancers Symposium, *J Clin Oncol* 2019.

Panagiotis J. Vlachostergios, Vincenza Conteduca, Amy Hackett, Jyothi Manohar, Aileen Lee, Aidan Case, Michael Sun, Muhammad J. Niaz, Olivier Elemento, Ana M. Molina, David M. Nanus, Himisha Beltran, Neil H. Bander, Scott T. Tagawa. Prognostic value of BRCA2 and AR gene alterations in advanced prostate cancer patients treated with PSMA-targeted radionuclide therapies. Presented at the 2019 AACR Annual Meeting.

Panagiotis J. Vlachostergios, Muhammad Junaid Niaz, Seyed Ali Mosallaie, Paul J. Christos, Amy Hackett, Joseph R. Osborne, Yuliya Jhanwar, Lauren Gracey, Ana M. Molina, David M. Nanus, Neil Harrison Bander, Scott T. Tagawa. Association of noninvasive, radiographic measurement of prostate-specific membrane antigen (PSMA) expression with response to PSMA-targeted radionuclide therapy (TRT). Presented during poster discussion session of the 2019 ASCO Annual Meeting, *J Clin Oncol* 2019

S.T. Tagawa, J. Osborne, A. Hackett, M.J. Niaz, V. Cooley, P. Christos, P. Vlachostergios, C. Thomas, L. Gracey, H. Beltran, A. Molina, D.M. Nanus, J. Babich, S. Vallabhajosula, A. O. Sartor, K. Ballman, N.H. Bander. Preliminary results of a phase I/II study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration resistant prostate cancer (mCRPC). Presented in poster discussion session of 2019 ESMO annual meeting. *Annals of Oncology* 2019

S.T. Tagawa, J. Osborne, M.J. Niaz, S. Vallabhajosula, P. Vlachostergios, C. Thomas, A. Molina, C.N. Sternberg, S. Singh, E. Fernandez, J. Babich, D.M. Nanus, K. Ballman, N.H. Bander. Dose-escalation results of a phase I trial of $^{225}$Ac-J591 for progressive metastatic castration-resistant prostate cancer (mCRPC). Presented at the 2020 Genitourinary Cancers Symposium, published in supplement to *J Clin Oncol.*

S.T. Tagawa, J. Osborne, C. Thomas, E. Fernandez, M.J. Niaz, S. Vallabhajosula, P. Vlachostergios, A. Molina, C.N. Sternberg, S. Singh, A. Patel, A. Tan, J. Babich, D.M. Nanus, K. Ballman, N.H. Bander. Phase I dose-escalation trial of prostate-specific membrane antigen (PSMA)-targeted alpha emiter $^{225}$Ac-J591 for progressive metastatic castration-resistant prostate cancer (mCRPC). Presented at the 2020 AACR Annual Meeting, published in Proceedings of the 2020 Annual Scientific Meeting of the American Association of Cancer Research.

Niaz MJ, Skafida M, Osborne J, Nanus DM, Molina AM, Thomas C, Vallabhajosula S, Christos P, Bander NH, Tagawa ST. (PD16-11) Comparison of prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy (TRT) with lutetium-177 ($^{177}$Lu) via antibody J591 vs small molecule ligand PSMA-617. Presented at the 2020 AUA annual meeting, published in supplement to *J Urol*.

S.T. Tagawa, J. Osborne, E. Fernandez, C. Thomas, M.J. Niaz, S. Vallabhajosula, P. Vlachostergios, A. Molina, C.N. Sternberg, S. Singh, J. Babich, D.M. Nanus, K. Ballman, N.H. Bander. Phase I dose-escalation study of PSMA-targeted alpha emiter $^{225}$Ac-J591 in men with metastatic castration-resistant prostate cancer (mCRPC). Presented at the 2020 ASCO Annual Meeting, published in supplement to *J Clin Oncol*.

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**Website(s) or other Internet site(s):** Nothing to report

**Technologies or techniques** Nothing to report

**Inventions, patent applications, and/or licenses** Nothing to report

**Other Products** Nothing to report

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

**What individuals have worked on the project?**

| | |
|---|---|
| Name: | Scott Tagawa |
| Project Role: | PI |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 0.3 |
| Contribution to Project: | Oversees the entire study |
| Funding Support: | Weill Cornell Medicine |

| | |
|---|---|
| Name: | Neil Bander |
| Project Role: | PI |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 0.3 |
| Contribution to Project: | Oversees entire study, esp immunologic and imaging components |
| Funding Support: | Weill Cornell Medicine |

| | |
|---|---|
| Name: | Himisha Beltran |
| Project Role: | PI |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 0.3 |
| Contribution to Project: | Oversees genomic portions of the project |
| Funding Support: | Dana Farber Cancer Institute |

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Dr. Tagawa has additional support (including PI and co-investigator on additional DOD grants), but without overlap or change in effort on this project.

Dr. Bander has additional involvement as co-investigator on another DOD grant, but with no overlap or change in effort on this project.

Dr. Beltran has additional involvement as co-investigator on another DOD grant, but with no overlap or change in effort on this project.

**What other organizations were involved as partners?** Nothing to report

## 8. SPECIAL REPORTING REQUIREMENTS

**COLLABORATIVE AWARDS: N/A**

**QUAD CHARTS: N/A**

## 9. APPENDICES:

N/A