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TITLE: Annotating MYC Status in Treatment-Resistant Metastatic Castration-Resistant Prostate Cancer with Gallium-68 Citrate PET

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

We are the first group to clinically investigate transferrin-based PET imaging in advanced prostate cancer with the use of gallium citrate PET as a non-invasive imaging biomarker of MYC activity. To date, we have successfully completed 40 whole body gallium citrate PET scans in 30 patients. 10 of the 30 patients enrolled have completed paired baseline and post-treatment initiation scans following treatment with either BET bromodomain inhibition or other standard of care therapies. We have successfully completed the interim analysis demonstrated acceptable safety of the imaging tracer and preliminary evidence of the diagnostic and predictive utility of gallum citrate PET in abiraterone-resistant metastatic castration resistant prostate cancer (mCRPC). Of the 30 patients enrolled, every patient has had at least one metastatic lesion detected on gallium citrate PET. Using analysis from paired metastatic tumor biopsies and circulating tumor DNA, we observe at interim analysis preliminary evidence of an association with MYC amplification, overexpression of MYC and downstream transcriptional targets including the transferring receptor (TFRC), as well as enrichment for higher level of avidity in patients with aggressive phenotypic prostate cancer, frequently with serologic or histologic evidence of small cell neuroendocrine features. To date, 10 patients have undergone paired Gallium citrate PET scans at baseline and following treatment initiation on a clinical trial of a BET bromodomain inhibitor. At the interim analysis, patients with a decrease from baseline in $SUV_{max\text{-}ave}$ on follow up Ga citrate PET have demonstrated a significantly longer time to disease progression compared to subjects with early increase in uptake on PET, demonstrating the potential utility as a predictive and pharmacodynamic biomarker in patients treated with BET inhibitor and other therapies targeting MYC-hyperactive advanced prostate cancer. Accrual is ongoing and we anticipate completion of study accrual within next 6-9 months.

15. SUBJECT TERMS

Prostate cancer; molecular imaging, biomarker, MYC oncogene, BET bromodomain inhibitor, castration-resistance, neuroendocrine prostate cancer

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1. INTRODUCTION:

The biology of metastatic castration-resistant prostate cancer (mCRPC) has shifted towards an aggressive phenotype with frequency neuroendocrine differentiation upon the emergence of resistance to abiraterone. There is an urgent unmet medical need to develop novel targeted anti-cancer therapies to improve survival for this oft-lethal disease subtype. Our preliminary data from patient-derived abiraterone-resistant metastatic tumor samples has identified significant up-regulation of the MYC oncogenic activity as a potential driver of therapeutic resistance. Emerging MYC-targeted therapies including bromodomain inhibition to down-regulate MYC expression are entering clinical studies in abiraterone-resistant mCRPC. **Critical to the successful development of MYC targeted therapies in mCRPC is the concurrent development of a functional biomarker of MYC activity to optimize dose and patient selection in early phase clinical trials. We have initiated the first-ever, proof-of-concept, translational study of gallium citrate PET as a non-invasive imaging biomarker of MYC activity for mCRPC patients receiving a next-generation potent bromodomain 4 (BRD4) inhibitor.**

Specific Aims:
(1) To compare ^{68}Ga-citrate uptake on PET imaging with level of MYC transcriptional activity assessed in abiraterone-resistant CRPC. Gallium citrate PET will be coupled with genomic analysis of mCRPC biopsies and circulating tumor DNA and tumor cells to validate Ga-68 citrate as functional biomarker of MYC oncogenic signaling.
(2) To perform first-ever proof-of-concept studies investigating the utility of Gallium citrate PET as a pharmacodynamic and predictive biomarker of MYC pathway inhibition in mCRPC. Correlative pre- and post-treatment Gallium citrate PET imaging will be integrated into an upcoming clinical trial at UCSF aimed at down-regulating MYC expression in mCRPC via BET inhibition (GS-5829).

2. KEYWORDS:

Prostate cancer; molecular imaging, biomarker, MYC oncogene, BET bromodomain inhibitor, castration-resistance, neuroendocrine prostate cancer

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major Task 1: Finalize Imaging Protocol and Preparation for Study Opening	Months	Status
Optimize time and dose of gallium citrate in mCRPC patients under existing pilot imaging study protocol	1-6	Completed
Quality assurance of gallium generator and verification of organ dosimetry	1-6	Completed
Finalize clinical trial agreements (CTAs) with Gilead Sciences	1-4	Completed
Draft and finalize imaging protocol and imaging manual	6-9	Completed
Draft and finalize laboratory manual including collection and processing of blood and tissue under auspices of WCDT protocol	1-6	Completed
Obtain UCSF IRB approval for companion imaging study of gallium citrate PET	6-9	Completed
Obtain Investigational New Drug (IND) application	6-9	Completed
Preparation of electronic case report forms within encrypted Oncore® database	6-9	Completed
Milestone Achieved: Finalization of study contract and budget	9	Completed
Milestone Achieved: Research staff trained	9	Completed
Milestone Achieved: First patient consented, screened, and enrolled on study	9	Completed

Major Task 2: Patient Accrual/Data Monitoring (N = 20 patients over months 9-28)	Months	Status
Weekly review of active study patients for adverse events/safety monitoring (N = 20 patients)	9-28	Ongoing
Clinical data entry into encrypted Oncore® database	9-28	Ongoing
Genomic analysis of tumor biopsies in collaboration with UC Santa Cruz	9-28	Ongoing
Gallium-68 citrate PET image processing and calculation of $SUV_{max\text{-}ave}$ across metastatic lesions	9-28	Ongoing
Monthly teleconference with Study Investigators	9-28	Ongoing
Data monitoring and auditing by independent Data Monitoring and Safety Committee	9-28	Ongoing
Interim safety and efficacy data analysis	15-18	Completed
Milestone Achieved: Interim safety and efficacy analysis completed	18	Completed
Monitor patient accrual and amend protocol to adjust eligibility criteria and study procedures as needed	18-28	Ongoing

Milestone Achieved: Last patient enrolled	28	Not yet completed

Major Task 3: Study Follow-Up and Data Analysis	Months	Status
Weekly safety review of patients continuing to receive protocol therapy	28-36	Not yet completed
Patient follow up until time of completion of follow up scan	28-36	Not yet completed
Milestone Achieved: Last patient completes study follow up scan	36	Not yet completed
Assess correlation between SUVmax on gallium citrate PET with tissue-based genomic markers of MYC pathway activation in conjunction with UC Santa Cruz bioinformatics group	32-36	Ongoing
Assess percent change from baseline on gallium citrate PET upon treatment with bromodomain inhibitor	32-36	Ongoing
Milestone Achieved: Complete statistical analysis of results	34	Not yet completed
Milestone Achieved: Publication of study results in peer reviewed medical journal	36	Partially completed

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) Major Activities:
In the last reporting period, we continued patient accrual onto the Gallium citrate PET imaging study in patients with abiraterone and/or enzalutamide-resistant metastatic castration resistant prostate cancer. We have successfully completed and passed our interim safety analysis. To date, we have enrolled 30 patients. The baseline characteristics of the patients are shown in Table 1 below. All 30 patients enrolled to date had metastatic castration resistant prostate cancer with prior resistance to abiraterone and/or enzalutamide at the time of study enrollment, per pre-specified eligibility criteria:

Table 1. Baseline Patient Characteristics

	Patient Cohort (N = 30)
Median age (range)	69 (53-90)
Race/Ethnicity (%)	

Caucasian	23 (77)
African-American	2 (7)
Asian	5 (17)
Gleason grade at diagnosis (%)	
6	2 (7)
7	13 (43)
≥ 8	15 (50)
Prior Therapy for mCRPC	
Abiraterone	25 (83)
Enzalutamide	18 (60)
Docetaxel	5 (17)
Radium-223	1 (3)
Median lab values at the time of Ga-citrate PET (range)	
PSA (ng/mL)	40.0 (2.1 – 3007)
LDH (IU/L)	166 (118 – 894)
Neuron specific enolase (ng/mL)	8.25 (< 5 – 34.3)
Chromogranin (ng/mL)	17 (2.4 – 174)

We have performed paired Ga citrate PET imaging at baseline and following initiation of BET inhibitor treatment (GS-5829 or ZEN-3694) in 10 patients (Specific Aim 2) out of 20 planned patients (see Results below).

2) Significant Results

In the last reporting period, we have completed the interim analysis for safety and diagnostic utility of Ga citrate PET. To date, there have not been any adverse effects attributable to the tracer injection or scan procedure. By virtue of detection of metastatic lesions in 100% of patients with mCRPC, we also cleared our pre-specified interim analysis for diagnostic utility of the PET imaging agent. The optimal dose of Ga citrate PET has been determined to be 7-10 mCi, and the optimal uptake time is 220 – 260 minutes. Positive PET uptake is defined as uptake higher than the mediastinal blood pool. We observe expected normal distribution of the tracer within the liver and excretion through the urinary tract **(Figure 1 below)**.

The summary statistics for the baseline gallium citrate PET data are shown below in **Table 2** (N = 29 evaluable patients to date). All 29 evaluable patients had at least one metastatic lesion detected on conventional imaging (CT chest/abd/pelvis + whole body bone scan) that was avid for Ga-citrate tracer on whole body PET performed within 12 weeks following conventional imaging. Overall, we have observed a significantly higher percentage of bone lesions that were PET-avid compared with soft tissue (visceral, lymph node) (mean percentage positive lesions 66.7% in the bone versus 32.5% in the soft tissue; $p = 0.021$). The exact mechanism for this difference remains to be explored but does not appear to be related to potential confounders

including tracer dose, uptake take, body surface area, and estimated creatinine clearance. The median SUV_{max} averaged across up to 5 metastatic lesions ($SUV_{max\text{-}ave}$) per patient was 5.41 (range 2.9 – 18.8). There was significant inter-tumoral heterogeneity of uptake within and across patients, likely reflective of true biologic diversity of regulators of transferrin receptor expression, inculding MYC transcriptional activity. Representative images demonstrating the inter-tumoral heterogeneity are shown in **Figure 1.**

Figure 1

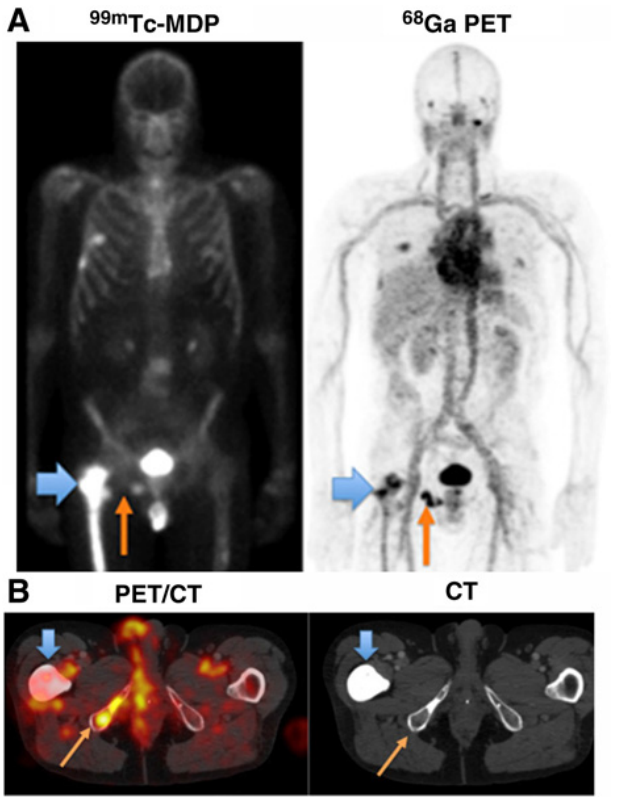

Figure 1. 68Ga-citrate uptake is heterogeneous among lesions detected with conventional imaging in the same patient. **A,** Multiple regions of uptake on 99mTc-HDP bone scan (left) including intense uptake in the right femur (blue arrow). Although the 68Ga-citrate PET MIP image (right) shows matching uptake in the right femur (blue arrow), it also reveals discordant uptake in the right ischium (orange arrow). **B,** Axial PET, CT, and fused 68Ga-citrate PET/CT through the right ischium show that the CT is normal in region of 68Ga-citrate uptake in the right ischium. CT also showing sclerosis in the region of the abnormal bone scan and 68Ga-citrate uptake (blue arrow).

Table 2. Summary Statistics for Baseline Ga-Citrate PET (N = 29 evaluable patients)

	Patient Cohort (N = 29 patients evaluable)
Median Dose of Ga citrate (mCi)	7.1 (3.7 – 10.8)
Median tracer uptake time (minutes)	221 (120 – 307)
Median number and distribution of PET avid lesions Total Bone lesions Soft tissue	 5 (1 – 29) 5 (1 – 29) 1 (0 – 3)
Mean percentage of PET avid lesions relative to conventional imaging (%) Total Bone Soft tissue	 60.3 (8.3 – 100) 66.7 (14.3 – 100) 32.8 (0 – 100)
Median $SUV_{max\text{-}ave}$ (range)	5.41 (2.9 – 18.8)

With respect to **Specific Aim 1**, we have observed preliminary evidence of correlation between MYC overexpression, along wth amplification of MYC in analysis of tumor DNA, in gallium citrate PET-avid lesions. Thus far, we have 20 patients evaluable for MYC amplification in analysis of circulating tumor DNA **(Table 3)**. Patients with hyperamplified MYC on analysis of circulating tumor DNA had a higher percentage of PET-avid metastatic lesions (68% vs. 47%, $p < 0.05$).

Table 3. MYC amplification by ctDNA analysis.

Samples	# of MYC copies gained	# of MYC copies gained, rounded
PC3 stock (+MYC) control	2.74	3
PC3 cfDNA (+MYC) control	1.58	2
Male germline DNA (WT MYC)	0	0
Patient-001	1.16	1
Patient-003	3.48	3
Patient-004	6.28	6
Patient-005	0.66	1
Patient-006	0.68	1
Patient-007	1.3	1
Patient-008	0.32	0
Patient-010	0.58	1
Patient-011	0.78	1
Patient-012	3.5	4
Patient-013	0.74	1
Patient-014	1.84	2
Patient-015	1.1	1
Patient-016	2.76	3
Patient-017	0.28	0
Patient-018	4.34	4
Patient-019	5.78	6
Patient-021	0.82	1

With respect to paired metastatic tumor biopsy, to date, 24 out of 30 patients enrolled have undergone a metastatic tumor biopsy following completion of Ga citrate PET. The median time interval between Ga citrate PET and subsequent metastatic tumor biopsy is 9 days. This short time interval between scan and paired tumor biopsy maximizes the chance for concordant findings to further probe the biologic underpinnings of Ga citrate tracer uptake on PET. The median SUV_{max} of the target lesion that has undergone paired tumor biopsy is 6.05 (range 1.7 – 10.8). The broad range of tracer uptake in the target lesion selected for paired tumor biopsy allows the possibility for the PETscan to capture varying degree of MYC expression, MYC transcriptional activity, and downstream expression of the transferrin receptor (TFRC) within the tumor. Currently, we have 10 evaluable biopsies with sufficient tumor that have undergone paired RNA sequencing. Though the sample size to date precludes definitive test for statistical correlation with sufficient power, we do observe a trend towards association between SUV_{max} of the target lesion on gallium citrate PET with MYC expression (expressed as the ratio of log transcript read of MYC to the housekeeper gene NADH) **(Figure 2)**.

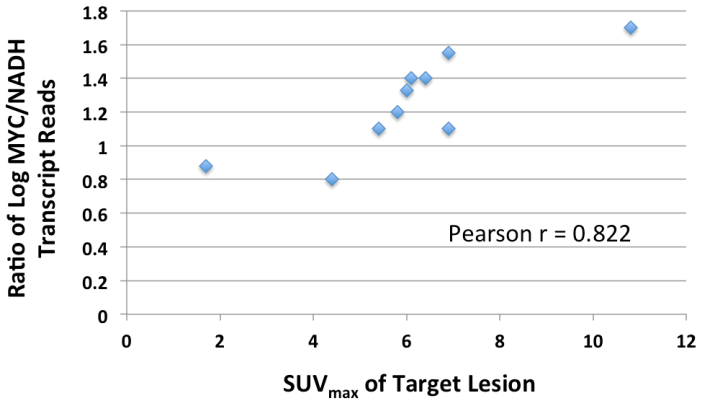

Figure 2. 68Ga-citrate uptake (SUVmax) in target lesion that underwent paired metastatic tumor biopsy and RNA-seq for transcriptional profiling of MYC and related genes. To date, 10 patients are evaluable for this analysis. There is preliminary evidence of correlation between SUVmax (x-axis) and ratio of log MYC/NADH transcript reads (y-axis) (Pearson r = 0.822).

With respect to completion of **Specific Aim 2**, we have have completed paired imaging with Ga citrate PET in 10 patinets before and following initiation of treatment with BET inhibitor on a clinical trial (GS-5829). The median time interval between the paired scans is 41 days (range 30-77). BET inhibition with GS-5829 has been confirmed to lead to a down-regulation of MYC expression in whole blood RNA analysis in a dose- and exposure-dependent manner, confirming the mechanism of action of this novel therapy **(Figure 3).**

Figure 3.

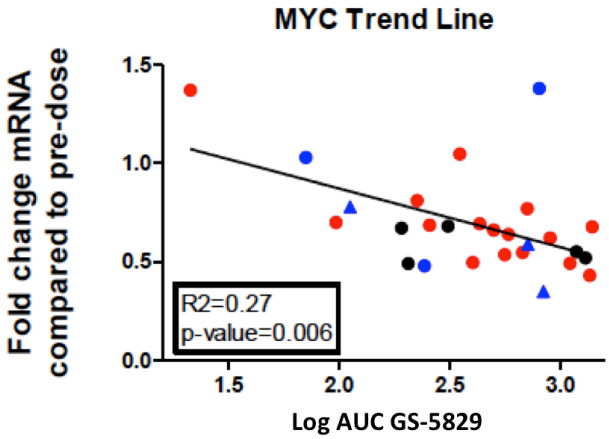

Figure 3. Fold change from baseline to end of week 4 in whole blood MYC expression. There is a dose dependent decrease in MYC expression upon treatment with BET inhibitor GS-5829.

On pre/post imaging with Ga-citrate PET, we have observed variable pattern with either increase or decrease in uptake. The mean percent change from baseline on follow up Ga citrate PET is -0.57%; however there is considerable inter-patient variability with the maximum decrease from baseline in $SUV_{max\text{-}ave}$ of -29.54% in a patient treated with GS-5829, who remained on study for > 12 months prior to progression. Intriguingly, a decline in uptake on follow up Ga-citrate PET is associated with a trend towards longer time to progression (median TTP = 9.4 months in those with decline from baseline on follow up PET versus median TTP of 3.5 months; log-rank p-value = 0.078). Therefore, early changes in Ga citrate PET may be a response prediction tool to guide the therapy of BET inhibitor and other MYC-targeting treatment strategies in advanced prostate cancer. This hypothesis is the subject of further investigation as we accrue additional patients to increase statistical power.

3) Other Achievements

Though not a formal Specific Aim of this grant, we have observed preliminary evidence supporting an association between uptake on Ga citrate PET with detection of treatment-emergent small cell neuroendocrine prostate cancer (t-SCNC). t-SCNC is an aggressive histologic subtype of prostate cancer with associated shortened survival outcomes (Aggarwal et al. J Clin Oncol 2018). In our multi-institutional Stand Up 2 Cancer cohort, we observed an incidence of t-SCNC of 17% in all metastatic castration resistant tumor biopsies. In the current analysis, we have observed a striking degree of uptake of Ga citrate PET in patients with histologic confirmation of small cell neuroendocrine prostate cancer. Of the 5 patients to date with histologic evidence of small cell neuroendocrine prostate cancer on paired tumor biopsy, the median SUV_{max} of the corresponding lesion on Ga citrate PET was 13.4 (7.3 – 18.8). Though the limited sample size precludes definitive comparison, the degree of uptake is numerically substantially larger than observed in the overall cohort and in the subset of patients without histologic evidence of t-SCNC. Furthermore, we have observed that paired Ga citrate PET is able to capture early metabolic response to platinum-based chemotherapy in a patient with t-SCNC treated with carboplatin + cabazitaxel **(Figure 4). These results will form the basis for our pending DOD Idea Expansion Grant application being submitted this Fall.**

Figure 4.

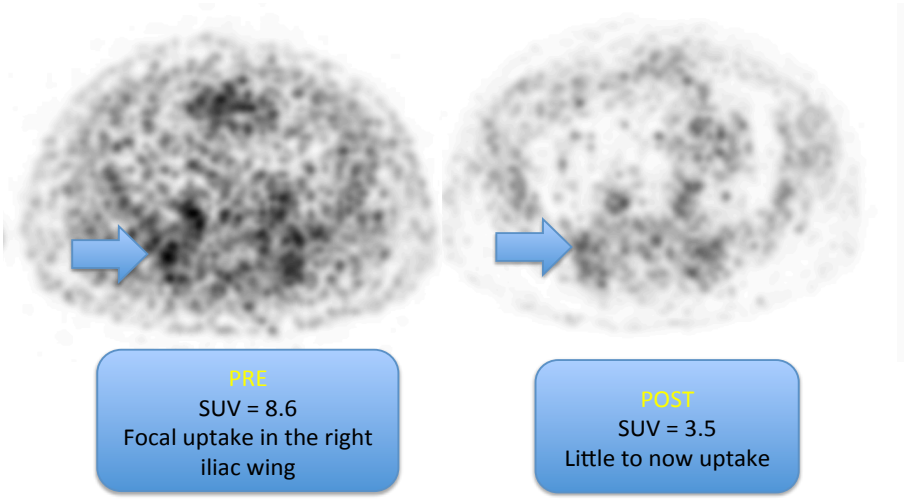

Figure 4. Paired Ga-citrate PET scans performed at baseline and following initiation of carboplatin + cabazitaxel chemotherapy in a patient with histologic evidence of small cell prostate cancer in a paired tumor biopsy of the R ilium. After just 1 cycle of treatment, and prior to any changes on conventional imaging or serologic markers (PSA, chromogranin, or neuron-specific enolase), there was significant down-regulation of uptake on follow up Ga-citrate PET performed using the same dose and uptake time of Ga-citrate.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to Report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We have presented findings to the Prostate Cancer Foundation Annual Scientific Meeting (2017) and plan to present an update at the 2018 meeting. We have also presented our findings to the Prostate Cancer Foundation Journal Club. We have additionally submitted UCSF press release announcing the publication of our pilot imaging study. We have had two manuscripts published since the grant inception, and a third manuscript describing the results discussed above is in the planning stages.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We aim to complete patient accrual with a target goal of 20 evaluable patients with paired Ga citrate PET imaging + RNA-sequencing and histologic classification data available from a paired tumor biopsy (Specific Aim 1). We aim to complete patient accrual to accrue 20 patients with evaluable serial Ga citrate PET scans performed before and following treatment initiation with a BET bromodomain inhibitor.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

The encouraging preliminary results demonstrating the feasiblity of gallium citrate PET imaging have spurred the incorporation of this imaging modality into other planned and ongoing clinical trials in metastatic prostate cancer patients, including upcoming study of the CDK 4/6 inhibitor ribociclib in combination with docetaxel (NCT02494921). We have also integrating paired imaging with gallium citrate PET into another Phase 1 clinical trial of an alternative BET bromodomain inhibitor, ZEN-003694 in combination with enzalutamide.

In addition, the imaging findings reported above have provided strong suppot for the use of Transferrin-based PET imaging in prostate cancer, and have spurred the clinical development of a second radiotracer, Zirconium-89 Transferrin, as an additional molecular imaging probe with the potential for a high degree of specificity and sensiivity in the detection of MYC-hyperactive mCRPC tumors. The planned first-in-human phase 1 pilot imaging study with this compound is scheduled to open to patient accrual in Q4 2017.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

The encouraging findings reported above have spurred the development of gallium citrate PET imaging in other malignancies with evidence of MYC hyperactivity, including glioblastoma and hepatocellular carcinoma.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

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5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report.

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

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals.

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  1. Aggarwal R, Behr S, Paris P, Truillet C Parker M, Huynh LT, Wei J, Hann B, Youngren J, Premasekharan G, Huang J, Ranatunga N, Chang E, Gao KT, Ryan CJ, Small EJ, and Evans MJ. Real time transferrin-based PET detects MYC-positive prostate cancer. Molecular Cancer Research 2017 [published online 7 June 2017].
  Acknowledgment of federal support: yes

  2. Behr S, Aggarwal R, Seo Y, Aparici CM, Chang E, Gao KT, Tao DH, Small EJ, and Evans MJ. A feasibility study showing 68Ga-Citrate PET detects prostate cancer. Molecular Imaging and Biology 2016;18(6):946-51.
  Acknowledgment of federal support: yes

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

1. Prostate Cancer Foundation Annual Scientific Meeting 2016, Carlsbad, CA
2. Prostate Cancer Foundation Annual Scientific Meeting 2017, Washington DC

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

The imaging methodology for gallium citrate PET imaging was published in our pilot imaging study as described above.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

The metastatic tumor biopsies that are being collected under the auspices of this grant will be broadly available for additional research inquiries, along with the clinical annotation of patient outcomes.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

1) Rahul Aggarwal
Project Role: Principal Investigator
Researcher Identifier (eRA Commons ID): RAHULA
Nearest person month worked: 1
Contribution to project: Dr. Aggarwal has served as Principal Investigator of the clinical imaging study of gallium citrate PET in mCRPC patients. He has been primarily responsible for patient accrual, data analysis, and coordination for acquisition of tissue/blood samples for the correlative studies. He has contributed to data analysis and manuscript preparation.

2) Spencer Behr
Project Role: Co-Investigator
Nearest person month worked: 1
Contribution to project: Dr. Behr is the principal nuclear medicine radiologist on the project. He has been responsible for the image analysis for summary of PET scan findings. He has been involved with data analysis and manuscript preparation.

3) Michael Evans
Project Role: Co-Investigator
Nearest person month worked: 1
Contribution to project: Dr. Evans is the chief laboratory investigator involved with the project. He has contributed to the data analysis and interpretation, along with preparation of manuscript.

4) Eric Small
Project Role: Co-Investigator
Nearest person month worked: 1
Contribution to project: Dr. Small has been the principal investigator for the biopsy acquisition protocol and has overseen efforts to obtain tissue and blood collection for the correlative assays for this proposal.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: N/A

9. APPENDICES:

None