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TITLE: Prospective-Retrospective Analysis of PTEN Immunohistochemistry Assay for Prediction of Outcomes in Recurrent and Metastatic Prostate Cancer

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14. ABSTRACT

As part of the CDMRP-funded Precision Medicine Biomarker Validating Center, we have developed a robust, highly analytically validated and cost-effective immunohistochemistry (IHC)-based assay to interrogate PTEN loss in prostate cancer. Our PTEN assay is prognostic in multiple cohorts of surgically-treated prostate cancer patients; now, we propose to leverage this body of previous validation studies to test the hypothesis that PTEN loss in primary prostate cancer predicts for a less robust response to hormonal therapies, in the context of two recent, practice-changing Phase III clinical trials for which we have CTEP approval to access specimens. Here, we report on progress to date. We have obtained tissue microarrays containing tissues from 306 patients for RTOG96-01 and immunostained them for PTEN and ERG. In initial analyses, patients with intact PTEN have a 50% decrease in cumulative incidence of metastasis with combined radiation therapy and anti-androgen therapy compared to radiation therapy alone, while patients with PTEN loss do not see the benefit of additional anti-androgen therapy.

15. SUBJECT TERMS
Prostate cancer, PTEN, ERG, immunohistochemistry, survival, radiation therapy, anti-androgen therapy

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1. INTRODUCTION:

With the completion of The Cancer Genome Atlas (TCGA) and Stand Up to Cancer (SU2C) sequencing projects for primary and metastatic prostate tumors, the genomic landscape of prostate cancer has largely been elucidated. Yet currently, none of the findings in these studies have improved patient outcomes in the disease, in large part because of the challenges associated with validating prognostic and predictive genomic biomarkers. Among the genomic changes cataloged, PTEN is the earliest and most commonly lost tumor suppressor in primary prostate cancers and its loss portends a poor prognosis and is associated with the development of castrate resistant disease in pre-clinical models. As part of the CDMRP-funded Precision Medicine Biomarker Validating Center, we have developed a robust, highly analytically validated and cost-effective immunohistochemistry (IHC)-based assay to interrogate PTEN loss in prostate cancer. Based on this work, these assays are currently performed in the Johns Hopkins CLIA/CAP-accredited Immunopathology Laboratory.

Hypothesis/Objective: Our PTEN assay is prognostic in multiple cohorts of surgically-treated prostate cancer patients; here, we will leverage this body of previous validation studies to test the hypothesis that **PTEN loss in primary prostate cancer predicts for a less robust response to hormonal therapies**, in the context of two recent Phase III clinical trials for which we have CTEP approval to access specimens.

Here, **we will test the hypothesis generated by preclinical models that PTEN loss predicts for a less robust response to AR-targeted and/or and androgen deprivation therapies**. More specifically, in the context of ECOG 3805, we will examine whether patients with PTEN-deficient metastatic prostate tumors derive additional benefit from docetaxel chemotherapy deployed with androgen deprivation therapy. In the context of RTOG 96-01, we will test whether the addition of AR-targeted therapy to radiation therapy is less beneficial for patients with patients with PTEN-deficient recurrent non-metastatic prostate tumors. In each study, we will further assess whether ERG status modulates the relationship of PTEN to clinical outcomes.

2. KEYWORDS:

Prostate cancer, PTEN, ERG, immunohistochemistry, survival, radiation therapy, anti-androgen therapy

3. ACCOMPLISHMENTS:

What were the major goals of the project?

a. **Specific Aim 1: Test whether PTEN status modifies benefit associated with treatment in ECOG 3805, a phase III trial that demonstrated a benefit for docetaxel chemotherapy at the time of starting androgen deprivation therapy (AAT) for men with high volume metastatic disease.**
    1. **Determine PTEN/ERG status of ~300 tumors from trial (~150 in each arm)**
        a. Obtain HRPO Approval for study (Hopkins IRB approval is in place already)
        b. Obtain tissue slides from ECOG in batches of 30
        c. Immunostain and blindly score for PTEN/ERG status

2. **Integrate PTEN/ERG status with de-identified clinical-pathologic data for study patients received from ECOG.** The primary objective will be to assess whether the relative benefit of docetaxel+AAT (androgen deprivation therapy) differs in patients with PTEN loss compared to PTEN intact. Secondary objectives will be to examine the association of PTEN status with outcome, stratified by treatment arm, ERG status, and/or low/high tumor volume.

b. **Specific Aim 2: Test whether PTEN status modifies the benefit associated with treatment in RTOG 96-01, a phase III trial that demonstrated a benefit for AR-targeted therapy with bicalutamide at the time of radiation therapy for non-metastatic PSA recurrence after radical prostatectomy.**

1. Construct Tissue microarray and determine PTEN/ERG status of ~550 tumors from trial

a. Obtain HRPO Approval for study (Hopkins IRB approval is in place already)
b. Generate tissue microarrays (TMAs) from 335 radical prostatectomy specimens in the study; receive ~212 slides of cases with slides available from NRG
c. Immunostain TMAs and tissue slides and blindly score for PTEN/ERG status

2. Integrate PTEN/ERG status with de-identified clinical-pathologic data for study patients received from NRG. The primary objective will be to assess PTEN status by immunohistochemistry (IHC) and assess whether PTEN status modifies the association of treatment (radiation therapy vs. radiation therapy+anti-androgen therapy) with metastasis free survival in patients treated with salvage radiation after biochemical recurrence. Secondary objectives will include similar evaluations of combined PTEN-ERG status, and whether PTEN or PTEN-ERG status are prognostic in these patients, independent of treatment. PTEN/ERG status may also be correlated with next generation sequencing data generated by the Maher-Feng-Tomlins study of the same specimens which is already approved

What was accomplished under these goals?

1) Major activities during this reporting period included a) analysis of ERG status from ECOG3805 and b) progress on studies involving RTOG96-01. In the previous reporting period, we described the analysis of PTEN data from ECOG3805. Here, we describe the ERG analysis and PTEN-ERG interaction analysis. Similarly, tissue microarrays containing 320 radical prostatectomies from patients in the trial were created by the RTOG tissue biorepository team from stored FFPE tissue blocks and stained and scored for PTEN and ERG and the data were presented in the previous progress report. In those data, we saw a trend that patients with PTEN loss may not derive the same benefit from addition of AAT to RT compared to patients with PTEN intact, as predicted by our hypothesis. However, because interaction analyses require a large sample size for power, we hoped that we might see a statistically significant interaction once we included additional cases which were provided by NRG from 163 cases where tissue blocks were not available, but unstained slides were stored for each patient. As planned, in the current period, these additional 163 cases with unstained standard slides available underwent immunostaining. We also worked to write a manuscript on the data previously reported from the ECOG3805 trial.

2) Specific objectives during this reporting period were to analyze the ERG data from ECOG3805 and to immunostain, score and analyze PTEN on 163 standard slides in the RTOG 96-01 trial. We also worked to write a manuscript on the data previously reported from the ECOG3805 trial.

3) Significant results or key outcomes:

a) **ERG analysis on ECOG3805:** ERG was positive in 40% of the ECOG3805 cohort (83/207) cases, as shown in Table 1. Clinical-pathologic variables were largely similar between the ERG positive and ERG negative subsets with the exception of vsiceral metastases which were more common in the ERG-negative subgroup. As seen in tables 1.1-1.16, ERG status was not significantly associated with outcomes in univariate or multivariate analysis. ERG was also not significantly associated with outcomes when examined in interaction with PTEN status, though the numbers analyzed may have been insufficient for this interaction analysis which requires large numbers of cases (see Tables 2.1-2.6).

ANALYSES OF ERG

Table 1. Comparison of variables stratified by ERG status

Variables	ERG negative (N=124)	ERG positive (N=83)	p-value
Age			0.567
N	124	83	
Median	63.5	63.0	
IQR	55.5-68.5	56.0-69.0	
Race – no. (%)			0.976
White	105 (84.7)	72 (86.8)	
Black	13 (10.5)	7 (8.4)	
Other	2 (1.6)	1 (1.2)	
Unknown	4 (3.2)	3 (3.6)	
Performance Status -- no. (%)			0.326
0	94 (75.8)	57 (68.7)	
1	29 (23.4)	26 (31.3)	
2	1 (0.8)	0 (0)	
Volume of disease -- no. (%)			0.773
Low	51 (41.1)	32 (38.6)	
High	73 (58.9)	51 (61.5)	
Visceral metastases -- no. (%)			0.016##

No Mets No Yes	51 (41.1) 50 (40.3) 23 (18.6)	32 (38.6) 46 (55.4) 5 (6.0)	
Gleason -- no. (%) 2-6 7 8-10	 6 (5.3) 32 (28.3) 75 (66.4)	 7 (8.9) 20 (25.3) 52 (65.8)	0.600
Baseline PSA N Median IQR	 123 37.9 11.8-191.0	 83 49.2 18.0-313.6	0.435
Prior RP -- no. (%) No Yes	 103 (83.1) 21 (16.9)	 63 (75.9) 20 (24.1)	0.205
Adjuvant ADT -- no. (%) No Yes	 117 (94.4) 7 (5.7)	 83 (100.0) 0 (0)	0.043
Assigned treatment -- no. (%) ADT alone ADT plus Docetaxel	 63 (50.8) 61 (49.2)	 44 (53.0) 39 (47.0)	0.756
Death -- no. (%) No Yes	 63 (50.8) 61 (49.2)	 46 (55.4) 37 (44.6)	0.515**
Prostate cancer death -- no. (%) No Yes Missing	 65 (54.6) 54 (45.4) 5	 51 (65.4) 27 (34.6) 5	0.133**
Follow up time* N Median IQR	 124 39.1 20.0-53.8	 83 42.1 29.6-57.8	0.162
CRPC -- no. (%) No Yes	 37 (29.8) 87 (70.2)	 29 (34.9) 54 (65.1)	0.440**

Time to CRPC[#]			0.152
N	124	83	
Median	14.2	17.8	
IQR	7.1-25.1	8.1-28.4	

* Months from randomization to death or censor
** Based on comparison of absolute proportions, not survival probability
# Months from randomization to CRPC
For ERG association with No mets or no visceral mets vs. visceral mets, p=0.005

MODELS OF ERG VS. OVERALL SURVIVAL

Table 1.1 Univariate Cox proportional hazards model of OS vs. ERG (n=207)

Variables	HR (95% CI), P-value
ERG	
negative	1
positive	0.79 (0.53-1.19), 0.260

Table 1.2. Cox proportional hazards model of OS vs. ERG, assigned treatment, and their interaction (n=207)

Variables	HR (95% CI)	p-value for adding treatment effect and interaction to ERG alone
ERG effect for ADT only		0.395 (Chi-square=1.856, 2 df*)
ERG positive vs. negative	1.03 (0.59-1.81)	
ERG effect for ADT+Docetaxel		
ERG positive vs. negative	0.59 (0.32, 1.08)	

***** Likelihood ratio test compared to model with ERG alone.

Table 1.3. Univariate Cox proportional hazards model of OS vs. ERG, for "assigned treatment"=ADT Alone (n=107)

Variables	HR (95% CI), P-value
ERG	
ERG negative	1
ERG positive	1.03 (0.59-1.80), 0.926

Table 1.4. Univariate Cox proportional hazards model of OS vs. ERG, for "assigned treatment"=ADT plus Docetaxel (n=100)

Variables	HR (95% CI), P-value
ERG	
ERG negative	1
ERG positive	0.58 (0.32-1.06), 0.076

Table 1.5. Cox proportional hazards model of OS vs. ERG, disease volume, and their interaction (n=207)

Variables	HR (95% CI)	p-value for adding disease volume to ERG alone
ERG effect for disease volume=LOW ERG positive vs. negative	1.05 (0.51-2.66)	0.254 (Chi-square = 1.30, 1 df*)
ERG effect for disease volume=HIGH ERG positive vs. negative	0.63 (0.38, 1.03)	

***** Likelihood ratio test compared to model with ERG and disease volume (without interaction).

Table 1.6. Univariate Cox proportional hazards model of OS vs. ERG, for disease volume=LOW (n=83)

Variables	HR (95% CI), P-value
ERG	
ERG negative	1
ERG positive	1.11 (0.54-2.28), 0.781

Table 1.7. Univariate Cox proportional hazards model of OS vs. ERG, for disease volume=HIGH (n=124)

Variables	HR (95% CI), P-value
ERG	
ERG negative	1
ERG positive	0.64 (0.39-1.06), 0.081

Table 1.8. Multivariable Cox proportional hazards model of OS vs. ERG, adjusted for baseline model clinical variables (n=192)

Variables	HR (95% CI), P-value
ERG	
negative	1
positive	0.72 (0.46, 1.13), 0.150
RP year, per year	0.999 (0.998, 1.00), 0.014
Visceral disease	
no mets (ref)	1
no visceral disease	1.52 (0.94, 2.44), 0.086
visceral disease	2.80 (1.47, 5.33), 0.002
Gleason score	
≤6 (ref)	1
7	0.87 (0.45, 1.69), 0.679
8-10	1.69 (1.01, 2.84), 0.045

MODELS OF ERG VS. CRPC (see Table 1.6 for baseline clinical model of CRPC)

Table 1.9. Univariate Cox proportional hazards model of CRPC vs. ERG (n=207)

Variables	HR (95% CI), P-value
ERG	
Negative	1
Positive	0.78 (0.55-1.10), 0.152

Table 1.10. Multivariable Cox proportional hazards model of CRPC vs. ERG, adjusted for baseline model clinical variables (n=192)

Variables	HR (95% CI), P-value
ERG	
Negative	1
Positive	0.75 (0.52, 1.07), 0.110
Prior RP (yes vs. no)	0.55 (0.33, 0.91), 0.021
Gleason score	
≤6 (ref)	1
7	1.35 (0.80, 2.26), 0.259
8-10	1.78 (1.16, 2.73), 0.008

Table 1.11. Cox proportional hazards model of CRPC vs. ERG, assigned treatment, and their interaction (n=207)

Variables	HR (95% CI)	p-value for adding treatment effect and interaction to ERG alone
ERG effect for ADT only ERG positive vs. negative	0.95 (0.60-1.51)	0.182 (Chi-square=3.41, 2 df*)
ERG effect for ADT+Docetaxel ERG positive vs. negative	0.62 (0.37, 1.03)	

* Likelihood ratio test compared to model with ERG alone

Table 1.12. Univariate Cox proportional hazards model of CRPC vs. ERG, for Assigned treatment=ADT alone (n=107)

Variables	HR (95% CI), P-value
ERG Negative Positive	 1 0.92 (0.58-1.47), 0.738

Table 1.13. Univariate Cox proportional hazards model of CRPC vs. ERG, for Assigned treatment=ADT +Docetaxel (n=100)

Variables	HR (95% CI), P-value
ERG Negative Positive	 1 0.64 (0.38-1.08), 0.092

Table 1.14. Cox proportional hazards model of CRPC vs. ERG, disease volume, and interaction (n=207)

Variables	HR (95% CI)	p-value for adding disease volume to ERG alone
ERG effect for disease volume=LOW ERG positive vs. negative	0.67 (0.37-1.20)	0.532 (LR Chi-square = 0.39, 1 df*)
ERG effect for disease volume=HIGH ERG positive vs. negative	0.84 (0.55, 1.28)	

***** Likelihood ratio test compared to model with ERG and disease volume (without interaction).

Table 1.15. Univariate Cox proportional hazards model of CRPC vs. ERG, for "volume of disease"=low (n=83)

Variables	HR (95% CI), P-value
ERG	
Negative	1
Positive	0.69 (0.39-1.25), 0.219

Table 1.16. Univariate Cox proportional hazards model of CRPC vs. ERG, for "volume of disease"=high (n=124)

Variables	HR (95% CI), P-value
ERG	
Negative	1
Positive	0.85 (0.56-1.30), 0.453

MODELS OF PTEN AND ERG COMBINED VS. OVERALL SURVIVAL

Table 2.1. Cox proportional hazards model of OS vs. PTEN, ERG, and their interaction (n=207)

Variables	HR (95% CI)	p-value for adding ERG and interaction to PTEN alone
PTEN effect for ERG negative		0.266 (Chi-square=2.65, 2 df*)
PTEN loss vs. intact	1.26 (0.76-2.08)	
PTEN effect for ERG positive		
PTEN loss vs. intact	0.78 (0.41, 1.48)	

***** Likelihood ratio test compared to model with PTEN alone.

Table 2.2. Univariate Cox proportional hazards model of OS vs. PTEN, for ERG negative (n=124)

Variables	HR (95% CI), P-value
PTEN	
PTEN intact	1
PTEN loss	1.29 (0.77-2.14), 0.332

Table 2.3. Univariate Cox proportional hazards model of OS vs. PTEN, for ERG positive (n=83)

Variables	HR (95% CI), P-value
PTEN	

PTEN intact	1
PTEN loss	0.75 (0.39-1.45), 0.395

MODELS OF PTEN AND ERG COMBINED VS. CRPC

Table 2.4. Cox proportional hazards model of CRPC vs. PTEN, ERG, and their interaction (n=207)

Variables	HR (95% CI)	p-value for adding ERG and interaction to PTEN alone
PTEN effect for ERG negative PTEN loss vs. intact	1.10 (0.72-1.68)	0.238 (Chi-square=2.87, 2 df*)
PTEN effect for ERG positive PTEN loss vs. intact	0.76 (0.44, 1.431)	

***** Likelihood ratio test compared to model with PTEN alone.

Table 2.5. Univariate Cox proportional hazards model of CRPC vs. PTEN, for ERG negative (n=124)

Variables	HR (95% CI), P-value
PTEN	
PTEN intact	1
PTEN loss	1.08 (0.70-1.66), 0.722

Table 2.6. Univariate Cox proportional hazards model of CRPC vs. PTEN, for ERG positive (n=83)

Variables	HR (95% CI), P-value
PTEN	
PTEN intact	1
PTEN loss	0.77 (0.45-1.33), 0.346

b) **Examination of PTEN/ERG status on standard slides of RTOG 96-01 cohort**: Unfortunately, we ran into a major quality issue with these standard slides which was not foreseen. Per Dr. Jeff Simko, the unstained slides were stored at an unknown temperature since the trial was started in 1998 until ~2010 when he received the cases and stored them at 4 degrees. Many of the patients had radical prostatectomies 5 years before this date, thus many samples are close to 25 years old at this point. When we received the standard slides, several of them were visibly moldy, suggesting storage in warm and moist conditions, which is suboptimal for pre-cut FFPE tissue sections. Our group has previously compared PTEN immunostaining for varying pre-analytic conditions and found that storage for 5 years at room temperature is acceptable for unstained slides, though there was some decrease in

staining intensity over this period (PMID: 30295067) however we did not examine time periods as long as 20 years which was likely the case with the RTOG 96-01 cases.

Strikingly, we found that PTEN staining was not interpretable in 78% of the 163 slides we received, due to complete absence of staining in both the internal control tissue (benign glands and stroma) and the sampled tumor cells. In only 35 cases were we able to score PTEN, with loss seen in 54% (19/35). This was in striking contrast to our previous results on cases in the tissue microarrays where FFPE blocks were available and stored for the same duration. In these cases, 99% (309/312) were interpretable for PTEN status.

To verify that this was a tissue-specific issue (and not due to our staining protocol), we reached out to Dr. Feng (co-I) who ran the testing of these same tissues for RNA expression profiling using the Decipher platform. They shared their data with us and we found that of the cases where FFPE blocks were available (and TMAs were made), RNA quality was acceptable in 90% (267/298) of cases where PTEN immunostaining was interpretable. Among cases with standard slides, RNA quality was only acceptable in 54% (18/33) of cases with interpretable PTEN immunostaining and 25% (31/124) cases with immunostaining failure. These data suggest a progressive decrement in RNA quality from TMAs to standard slides, with an even more dramatic decrease among the standard slides where PTEN staining failed. These data strongly point to a significant pre-analytic issue in the stored standard slides.

To begin to address this, we have been working to boost the signal in our PTEN immunostain. Working with Dr. De Marzo (co-I on this award), we stained a subset of 20 cases using a PTEN immunostaining protocol that employs tyramide amplification on the automated Ventana platform. Unfortunately, the amplified stain was interpretable in only 2/20 cases. We are currently working to determine whether other amplification reagents and variations on the tyramide amplification protocol may be more successful. Due to these issues, we have held off on completing ERG immunostaining on the 163 standard slides as we have only a single slide remaining to test and we want to make sure we do not need this slide for repeat PTEN staining should we be able to improve the protocol. However, ERG immunostaining was performed as planned on the tissue microarray cohort and reported in the previous progress report. Bruce Trock will perform interaction analyses with the PTEN and ERG results once they are complete for the cohort to see if they interact to predict patient prognosis (secondary objective).

Finally, we have written a manuscript reporting the complete PTEN/ERG immunostaining data from the ECOG3805 trial and this is pending submission in the next few weeks.

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

Nothing to report

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

In the no cost extension period for this award, we will focus on performing and analyzing the ERG immunohistochemistry for RTOG96-01. If feasible, we will redo the PTEN staining on cases that have failed using an amplification protocol, however to date we have been unable to get one to work. In addition, we will examine the interaction between PTEN and ERG with therapy arm in RTOG96-01. Finally, we will write a manuscript describing the RTOG96-01 data for submission and work on any necessary revisions for the aforementioned ECOG3805 manuscript which should be under review shortly.

IMPACT

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

We have successfully determined PTEN and ERG status on the landmark ECOG3805 trial, where we did not see the expected effects of PTEN status on outcome, nor on interaction with therapy arm or ERG. For the RTOG96-01 trial, we see a trend that patients with PTEN loss may not derive the same benefit from addition of AAT to RT compared to patients with PTEN intact. If replicated in the additional samples (and statistically significant), these results suggest that PTEN may useful to determine which patients should get AAT when undergoing RT for biochemical recurrence after radical prsotatectomy. Given that AAT is associated with significant morbidity, biomarker selection could significantly improve patient case in this setting. These data are awaiting additional samples where staining will need to be redone due to pre-analytic variables.

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

4. CHANGES/PROBLEMS

Changes in approach and reasons for change

As described above, many of the RTOG 96-01 samples were of poor quality due to long-term storage at room temperature. We are working on changing and revalidating the staining protocol to amplify the signal in these cases. There is no change to budget or statement of work at this point.

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

We had a research slowdown for three months from early March as the research labs were largely closed at Johns Hopkins, however we have made up for this lost time over the summer.

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

Nothing to report

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

5. **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

An abstract describing the RTOG96-01 work was presented at USCAP (United States and Canadian Association of Pathology) 2020 meeting. Data were also presented at the December 2020 NRG meeting in Denver, CO.

Journal publications.

We are finishing a manuscript on ECOG3805 for publication as described above.

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers, and presentations.

Nothing to report

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
Database of PTEN/ERG status in ECOG3805 and RTOG 96-01 trial patients. We will make this available to other researcher upon publication via ECOG and NRG.

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	*Tamara Lotan*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	*Tlotan1*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Lotan supervised IHC data collection and interpretation.*
Funding Support:	*NCI/NIH, CDMRP-PCRP*

Name:	*Sanjana Murali*
Project Role:	*Research technician*
Researcher Identifier (e.g. ORCID ID):	*NA*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Murali performed IHC staining.*
Funding Support:	*CDMRP-PCRP*

Name:	*Daniela Salles*
Project Role:	*Postdoctoral fellow*
Researcher Identifier (e.g. ORCID ID):	*NA*
Nearest person month worked:	*4*
Contribution to Project:	*Dr. Salles performed IHC data collection and interpretation.*
Funding Support:	*CDMRP-PCRP*

Name:	*Bruce Trock*
Project Role:	*Co-investigator*
Researcher Identifier (e.g. ORCID ID):	*Btrock1*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Trock performed statistical data analysis*
Funding Support:	*NCI/NIH, CDMRP-PCRP*

Name:	*Angelo De Marzo*
Project Role:	*Co-investigator*
Researcher Identifier (e.g. ORCID ID):	*Ademarz1*
Nearest person month worked:	*<1*
Contribution to Project:	*Dr. De marzo assisted with IHC interpretation and data analysis interpretation*
Funding Support:	*NCI/NIH, CDMRP-PCRP*

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

Changes to Dr. Lotan's other support since last report are as follows:

National Institutes of Health - # R01CA211695 – Completed

National Institutes of Health - # R01CA200859 – Completed

National Institutes of Health - # R01CA238218 – Completed

Department of Defense - W81XWH-16-1-0737 – Completed

American Cancer Society - #RSG-17-160-01-CSM – Completed

Department of Defense - #W81XWH-19-1-0292 – Active

Department of Defense - #W81XWH-19-1-0781 – Active

Department of Defense - #W81XWH-19-1-0345 – Active

Department of Defense - #W81XWH-19-1-0686 – Active

Department of Defense - W81XWH-20-1-0177 – Active

Department of Defense - W81XWH-20-1-0254 – Active

Fidelity Charitable - #90087049 – Active

Prostate Cancer Foundation - #19CHAS03 – Active

National Institutes of Health - # R01CA238284 – Active

What other organizations were involved as partners?

Organization Name: University of California San Francisco

Location of Organization: San Francisco, CA

Partner's contribution to the project

Collaboration : Dr. Felix Feng is a radiation oncologist who contributed to interpretation of the RTOG9601 data as described above. He is in charge of the GU Translational Research Program at NRG. Dr. Feng helped with approvals through NRG and with interpretation of the data.

Organization Name: Dana Farber Cancer Institute

Location of Organization: Boston, MA

Partner's contribution to the project

Collaboration : Dr. Chris Sweeney is an oncologist who was PI of the ECOG3805 trial. He assisted with data interpretation and analysis and contributed to manuscript.

7. SPECIAL REPORTING REQUIREMENTS

Nothing to report

8. APPENDICES: None