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TITLE: Treatment Options and Survival of Metastatic Prostate Cancer Patients

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CONTRACTING ORGANIZATION: Washington University, Saint Louis, MO

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14. ABSTRACT

In this proposal, we will utilize a prostate cancer cohort from the VA hospitals to explore the survival benefit among men diagnosed with metastatic prostate cancer who receive definitive treatment (alone or with adjuvant therapies) compared to men who receive non-definitive treatment; and we will assess the treatment related side effects that affect quality of life among men diagnosed with metastatic prostate cancer who receive definitive vs. non-definitive treatment. The specific aims are:
Aim 1: To examine the survival benefit among men diagnosed with metastatic prostate cancer that receive definitive treatment compared to men that receive non-definitive treatment.
Aim 2: To examine treatment-related side effects that affect quality of life (impotence, incontinence and pain) among men diagnosed with metastatic prostate cancer that receive definitive treatment compared to men that receive non-definitive treatment.

15. SUBJECT TERMS

Prostate cancer, disparities, treatment, VHA, VACCR, survival, mortality, recurrence

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1. **INTRODUCTION:**
The objective of this study is to build on the comprehensive data that has been cultivated through the Health Disparity award and expand it to explore survival and quality of life benefits of definitive and non-definitive treatment combinations. In the study proposed here, we will abstract additional individual-level data on all treatments received including dates to assess timing of treatment, clinical assessment and/or diagnoses of treatment-related side effects that affect quality of life such as impotence, incontinence and pain. The additional data abstraction will also allow for the creation of comprehensive covariates including co-morbidity scores that contribute to survival in a metastatic prostate cancer population.

2. **KEYWORDS:**
Prostate cancer, disparities, treatment, VHA, VACCR, survival, mortality, recurrence

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

1. Team Meeting
   i. Review grant and progress of recruitment in parent study – Year 1, Month 1 – 100%
   ii. Team Meetings will occur monthly throughout the award – Year 1-3, Monthly – 100%
   iii. Interview and hire staff – Year 1, Month 2 – 100%
2. Regulatory review and IRB
   i. Complete and submit forms for regulatory review – Year 1, Months 1-2 – 100%
   ii. Complete and submit IRB forms for review – Year 1, Months 2-3 – 100%
   iii. Obtain approval for regulatory and IRB forms – Year 1, Month 4 – 100%
3. Study team will abstract and clean data
   i. Develop data abstraction form – Year 1, Months 3-5 – 100%
   ii. Abstract data – Year 1, Month 4-6 – 50%
   iii. Run frequencies, report, and correct any errors found – Year 1, Month 4-6 – 100%
4. Perform analyses
   i. Finalize data analysis plans – Year 1, Months 7-10 – 100%
   ii. AIM 1 – Yr 1: 10-12 – Yr 2: 1-2 – 100%
   iii. AIM 2 – Year 2, Months 3-6 – 75%
5. Manuscript Development
   i. AIM 1 –Year 2, Months 3-8 – 75%
   ii. AIM 2 – Year 2, Months 9-12; Year 3, Months 1-3 – 10%
   iii. Additional analyses– Year 3, Months 3-6 – 25%
6. Presentations – Years 2-3 – 10% complete
7. Community Input/Feedback – Years 1-3 – 60%
8. Planning for next study – Year 3, Months 6-12 – 25%

What was accomplished under these goals?

1. Major activities: Data activities included: established regular team meetings, hired statistician, achieved IRB approval, updated data with an additional year of diagnoses and vital status data, developed data abstraction form, ran frequencies and corrected errors, finalized variable definitions. We completed data abstraction and data analyses for each of the aims and finalizing the first manuscript which will be submitted in the next two months.
2. Specific objectives to be completed this year: Complete manuscripts for aims 2 and 3 and begin planning for subsequent research projects. In addition we have submitted abstracts for conference presentations in the upcoming year.
3. Significant results or key outcomes: See tables 1 and 2 below.

Table 1. Patients' characteristics of men diagnosed with metastatic [a] prostate cancer at the Veterans Health Administration between 1999-2013, by receipt of definitive prostate cancer treatment

		Metastatic Cancer: T4, M1, or N1				Metastatic Cancer: T4 or M1			
		Cohort	Non-definitive Treatment [b]	Definitive Treatment [c]	p-value [d]	Cohort	Non-definitive Treatment [b]	Definitive Treatment [c]	p-value [d]
		N=2919	N=1925	N=994		N=1479	N=1240	N=239	
		N (%)	**N (%)**	**N (%)**		**N (%)**	**N (%)**	**N (%)**	
Days from diagnosis to first treatment,					<0.0001				0.0604
<= Median		1461 (50.05)	1024 (53.19)	437 (43.96)		747 (50.51)	613 (49.44)	134 (56.07)	
> Median		1458 (49.95)	901 (46.81)	557 (56.04)		732 (49.49)	627 (50.56)	105 (43.93)	
Grade					0.0097				0.4068
	1	7 (0.24)	6 (0.31)	1 (0.10)		6 (0.41)	6 (0.48)	0 (0)	
	2	214 (7.33)	153 (7.95)	61 (6.14)		130 (8.79)	109 (8.79)	21 (8.79)	
	3	2592 (88.80)	1684 (87.48)	908 (91.35)		1276 (86.27)	1065 (85.89)	211 (88.29)	
	4	106 (3.63)	82 (4.26)	24 (2.41)		67 (4.53)	60 (4.84)	7 (2.93)	
Age					<0.0001				<0.0001
<50		48 (1.64)	19 (0.99)	29 (2.92)		16 (1.08)	9 (0.73)	7 (2.93)	
≥50- <60		570 (19.53)	294 (15.27)	276 (27.77)		228 (15.42)	171 (13.79)	57 (23.85)	
≥60-<70		1203 (41.21)	678 (35.22)	525 (52.82)		522 (35.29)	413 (33.31)	109 (45.61)	
≥70		1098 (37.62)	934 (48.52)	164 (16.50)		713 (48.21)	647 (52.18)	66 (27.62)	
Race					0.2187				0.714
White		2082 (71.33)	1354 (70.34)	728 (73.24)		1032 (69.78)	860 (69.35)	172 (71.97)	
Black		814 (27.89)	554 (28.78)	260 (26.16)		435(29.41)	370 (29.84)	65 (27.20)	
Other		23 (0.79)	17 (0.88)	6 (0.60)		12 (0.81)	10 (0.81)	2 (0.84)	
PSA					<.0001				<0.0001
0-<20		1332 (45.63)	635 (32.99)	697 (70.12)		532 (35.97)	398 (32.10)	134 (56.07)	
≥20		1587 (54.37)	1290 (67.01)	297 (29.88)		947 (64.03)	842 (67.90)	105 (43.93)	
Location					0.0017				0.2983
Urban		**2165 (74.17)**	1463 (76.00)	702 (70.62)		1110 (75.05)	937 (75.56)	173 (72.38)	
Rural		**754 (25.83)**	462 (24.00)	292 (29.38)		369 (24.95)	303 (24.44)	66 (27.62)	
Pca-Death (censored at 10 yr)					<0.0001				0.0033

Yes	**1281 (43.88)**	1041 (54.08)	240 (24.14)		809 (54.70)	699 (59.37)	110 (46.03)	
No	**1638 (56.12)**	884 (45.92)	754 (75.86)		670 (45.30)	541 (43.63)	129 (53.97)	
All death (censored at 10 yr)				<0.0001				<0.0001
Yes	**1909 (65.40)**	1500 (77.92)	409 (41.15)		1170 (79.11)	1013 (81.69)	157 (65.69)	
No	**1010 (34.60)**	425 (22.08)	585 (58.85)		309 (20.89)	227 (18.31)	81 (34.31)	
Charlson comorbidity index	**1.39 (1.71)**	1.55 (1.82)	1.09 (1.44)	<0.0001	1.50 (1.77)	1.56 (1.79)	1.22 (1.63)	0.0077

[a] Metastatic cancer was defined in two ways: (1) Men diagnosed with T4, M1, or N1 prostate cancer or (2) men diagnosed with T4 or M1 prostate cancer

[b] Non-definitive treatment was defined as receipt of any other therapy other than surgery (radical prostatectomy or radiation)

[c] Definitive treatment is defined as receipt of surgery (radical prostatectomy) or radiation, either alone or adjuvantly with other therapies

[d] p-value determined using chi-square test for continuous variables and t-test for categorical variables

Table 2. Inverse probability of definitive treatment weighted survival analyses: overall mortality and prostate cancer-specific mortality among men diagnosed with metastatic prostate cancer at the Veterans Health Administration between 1999-2013

		T4M1N1 (n=2,919)
		Definitive vs. Non-definitive
All-cause mortality	≤10 years	0.57 (0.61, 0.65)
Pca-specific mortality	≤10 years	0.50 (0.46, 0.55)
		T4M1 (n=1,479)
		Definitive vs. Non-definitive
All-cause mortality	≤8 years	0.84 (0.77, 0.91)
	8~10 years	3.33 (2.19, 5.05)
Pca-specific mortality	≤8 years	0.81 (0.73, 0.90)
	8~10 years	3.05 (1.73, 5.35)

Inverse probability of treatment weighted survival analyses adjusting for years from prostate cancer diagnosis to first treatment (<= median and > median), Grade (1,2,3,4), age at diagnosis (<50, ≥50-<60, ≥60-<70, ≥70), race (White, Black, Other), PSA at diagnosis (0-20, >20), and location (urban, rural) and comorbidity index without malignancy.

4. Other achievements: Most of the stated goals for the SOW have been met. It took a little longer than expected to hire a biostatistician; however, we were able to add Mei Wang to the team who started with experience and access to analyze VA data. Analysis paused in March 2020 when the institution instituted work from home. However, we were able to set up and utilize remote access to the VA server. Response times to data requests are longer than usual; however, we are able to continue our monthly meetings, contribute data abstraction, data analyses and draft manuscripts.

What opportunities for training and professional development has the project provided?
Through this project we have provided training on data abstraction and coding assistance to other VA cancer investigators conducting research using VAMC clinical data.

How were the results disseminated to communities of interest?
Dr. Drake presented an update of the data analyses from this project to the Epidemiology and Clinical Research group at the VA Medical Center.

What do you plan to do during the next reporting period to accomplish the goals?
We will continue to meet monthly as a team using zoom to accommodate variations in in-person and at-home status of faculty and staff to discuss the process of data abstraction, data analysis, and manuscripts writing. We will review the SOW regularly to ensure we stay on track.

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?
Nothing to report

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

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
Problem: Work from home order to due COVID-19 leads to slower response times and virtual team meetings.
Solution: All of our data requests have been submitted and our team will continue to meet via Zoom, virtually, to keep the project moving forward.

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
Nothing to report

Significant changes in use of biohazards and/or select agents
Nothing to report

6. **PRODUCTS:**

Publications, conference papers, and presentations

- **Journal publications.**
  Nothing to report

- **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
Nothing to report

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

What individuals have worked on the project?

Name:	Bettina F. Drake, PhD, MPH
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	0000-0001-9340-5848
Nearest person month worked:	5
Contribution to Project:	Dr. Drake is the lead investigator on this study
Funding Support:	DOD grant
Name:	Su-Hsin Chang, PhD
Project Role:	Co-I
Researcher Identifier (e.g. ORCID ID):	0000-0001-5872-9556
Nearest person month worked:	4
Contribution to Project:	Dr. Change has expertise in treatment effect evaluation and extensive experience using data from the Veterans Health Administration (VHA) to study obesity and cancer.
Funding Support:	DOD grant
Name:	Eric Kim, MD
Project Role:	Co-I
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	Dr. Kim will provide prostate cancer clinical expertise to the study team.
Funding Support:	DOD grant
Name:	Mei Wang, MS
Project Role:	Statistician
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	Ms. Wang will perform all data cleaning and statistical analysis for the project
Funding Support:	DOD grant

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
None

What other organizations were involved as partners?
Nothing to report

8. **SPECIAL REPORTING REQUIREMENTS**

COLLABORATIVE AWARDS:

N/A

QUAD CHARTS:

N/A

9. **APPENDICES:**

None