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TITLE: Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies

PRINCIPAL INVESTIGATOR: David Nanus

CONTRACTING ORGANIZATION: Weill Medical College of Cornell University

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The Weill Cornell Medical College Prostate Cancer Research Program (WCMC-PCRP) is a Clinical Research Site of the Prostate Cancer Clinical Trials Consortium (PCCTC). The objective of this research is for WCM, together with NYPBMH and CUMC, to participate in the PCCTC as a multisite Clinical Research Site. Our overall aim is to translate our prostate cancer expertise in targeted therapies, PC imaging, immunotherapy, and correlative science into novel therapeutic approaches that can be tested in multi-institutional studies performed within the PCCTC. We intend to bring novel agents and new biomarker-driven trials directly to PC patients, including underrepresented minorities. Our specific aims are 1) to develop and study novel, targeted therapeutics identified through high-quality molecular analyses; 2) to identify effective treatments and biomarkers based on discovery of mechanisms of PC therapy resistance and sensitivity; 3) to advance PC immunotherapeutics based on pre-clinical investigations; 4) to study PSMA-targeted radionuclide therapy and develop PSMA molecular imaging; and 5) to open up PCCTC studies to underrepresented minorities in Brooklyn and Upper Manhattan.

15. SUBJECT TERMS
None listed.

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1. **INTRODUCTION:**

The Weill Cornell Medical College Prostate Cancer Research Program (WCMC-PCRP) is a Clinical Research Site of the Prostate Cancer Clinical Trials Consortium (PCCTC). The objective of this research is for WCM, together with NYPBMH and CUMC, to participate in the PCCTC as a multisite Clinical Research Site. Our overall aim is to translate our prostate cancer expertise in targeted therapies, PC imaging, immunotherapy, and correlative science into novel therapeutic approaches that can be tested in multi-institutional studies performed within the PCCTC. We intend to bring novel agents and new biomarker-driven trials directly to PC patients, including underrepresented minorities. Our specific aims are 1) to develop and study novel, targeted therapeutics identified through high-quality molecular analyses; 2) to identify effective treatments and biomarkers based on discovery of mechanisms of PC therapy resistance and sensitivity; 3) to advance PC immunotherapeutics based on pre-clinical investigations; 4) to study PSMA-targeted radionuclide therapy and develop PSMA molecular imaging; and 5) to open up PCCTC studies to underrepresented minorities in Brooklyn and Upper Manhattan.

2. **KEYWORDS:**

Biomarkers, clinical trials, immunotherapy, monoclonal antibody, neuroendocrine prostate cancer, next-generation sequencing, prostate cancer, Prostate Cancer Clinical Trials Consortium, prostate specific membrane antigen, radionuclide therapy, translational research program.

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

SOW Major Task 1: Completion of regulatory review, Clinical Trial Startup
SOW Major Task 2: Adhere to performance metrics defined by Coordinating Center
SOW Major Task 3: Full participation in the consortium as a member of the Clinical Consortium Committee/Scientific Oversight Committee
SOW Major Task 4: Propose clinical trials to Consortium
SOW Major Task 5: Interim data analysis
SOW Major Task 6: Open other Consortium sponsored Clinical Trials at WCM
SOW Major Task 7: Clinical trial performance
SOW Major Task 8: Analysis and reporting of data

What was accomplished under these goals?

SOW Major Task 1. Completion of regulatory review, Clinical Trial Startup

Subtask 1 (Initiate and complete contractual agreements between PCCTC LLC with NYPBMH and CUMC): Completed.
Subtasks 2 thru 4: (Submission of protocols for scientific (BMH and CUMC) Protocol Review and IRB Submission; Clinical trial approval at BMH and CUMC; Site initiation visits):
Completed for many protocols. Other protocols at WCM, CU and at BMH and are in various stages of review and start up.

SOW Major Task 2: Adhere to performance metrics defined by Coordinating Center

Subtask 1. Accrue at least 25 patients/year to PCCTC trials across sites:

Ninety (90) patients have enrolled to 11 PCCTC protocols in this reporting period including 30 patients to the Ironman Registry. Total enrollment number for the PCCTC trials are below in the Table.

Study Title	WCM PI or Collaborator	Study Status	Enrollment
Phase I Trial of ARN-509 plus Abiraterone acetate, Docetaxel, and Prednisone in Patients with mCRPC (c15-163)	PI	Closed to enrollment	5
Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive mCRPC [c17-199]	PI	Open to enrollment	2

Phase I dose−escalation trial of 225Ac−J591 in patients with mCRPC [c18-218]	PI	Open to enrollment	8
Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (IRONMAN) c16-170	Collaborator	Open to enrollment	30
Randomized Phase 1b/2 Study of Nivolumab or Nivolumab Plus BMS-986253 in Combination with Intermittent Androgen Deprivation Therapy in Men with Hormone-Sensitive Prostate Cancer [18-229]	PI	Open to enrollment	19
A Randomized Phase II Trial of Abiraterone, Olaparib, or Abiraterone + Olaparib in Patients with mCRPC with DNA Repair Defects (c16-168: BRCAAway)	Collaborator	Open to enrollment	2
A Salvage Trial of AR Inhibition with ADT and Apalutamide with Radiation therapy followed by Docetaxel in Men with PSA Recurrent Prostate Cancer after Radical Prostatectomy (STARTAR) [c16-180]	Collaborator	Closed to enrollment	1
Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 for mCRPC (DORA) [c16-174]	Collaborator	Open to enrollment	3
A Single-arm, Phase 2 Study to Evaluate the Safety and Efficacy of IMMU-132 in Patients with Metastatic Castration-Resistant Prostate Cancer Who Have Progressed on Second Generation AR-Directed Therapy [c18-204]	Collaborator	Open to enrollment	3
Harpoon: A Phase 1 Open-label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability, and Pharmacokinetics of HPN424 in Patients with Advanced Prostate Cancer Refractory to Androgen Therapy [c20-257]	PI	Open to enrollment	13
UWash: A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors [c20-259]	Collaborator	Open to enrollment	4
Total:			90

Subtask 2. Accrue at least 5% of patients from disproportionately affected populations per year across sites.

26 of 90 patients (28.8%) were from disproportionately affected populations. In addition, 12 patients to date of the 90 enrolled were United States Veterans.

Demographic	African American	White NH	White H	Asian	Other / Unknown	Total Subjects in Year
Year 2 10/1/19-9/30/20	8	61	15	3	3	90
	8.8%	67.7%	16.6%	3.3%	3.3%	

Subtask 3. Propose > 2 clinical trials per year or 6 trials over 3 years for consideration by the consortium, which may include biomarker studies.

We have opened or will shortly propose to the consortium nine clinical trials for which we serve as principle investigator (listed below).

Study Title
IIT CUMC Magic 8 - Randomized Phase 1b/2 Study of Nivolumab or Nivolumab Plus BMS-986253 in Combination with Intermittent Androgen Deprivation Therapy in Men with Hormone-Sensitive Prostate Cancer [c18-229] -PI Charles Drake M.D, Ph.D
Phosplatin Therapeutics: A phase 1, open-label, study evaluating the safety, pharmacokinetics, and clinical effects of intravenously administered PT-112 injection in subjects with advanced solid tumors – PI Scott Tagawa M.D.
IIT An Open Label, Non-Randomized Phase II Trial of Cabozantinib in Patients with Metastatic CRPC and Known Amplifications or Activating Mutations in Gene Targets of Cabozantinib – PI David Nanus M.D.
IIT 225-AC-J591+Pembro: Phase I/II of pembrolizumab and androgen-receptor pathway inhibitor with or without 225Ac-J591 for progressive metastatic castration resistant prostate cancer -PI Scott Tagawa M.D.
IIT Whole Food Plant Based Diet: Whole-Food Plant-Based Diet (WFPBD) to Control Weight and Metabo-Inflammation in Overweight/Obese Men with Prostate Cancer Receiving Androgen Deprivation Therapy (ADT): A Multi-Center Randomized Control Trial -PI David Nanus M.D.
Harpoon: A Phase 1 Open-label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability, and Pharmacokinetics of HPN424 in Patients with Advanced Prostate Cancer Refractory to Androgen Therapy -PI Mark Stein M.D
IIT Actinium: Phase I dose−escalation trial of 225Ac−J591 in patients with metastatic castration−resistant prostate cancer [c18-218] -PI Scott Tagawa M.D
IIT PSMA 617 Fractionated: Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration resistant prostate cancer [c17-199] -PI Scott Tagawa M.D

IIT Janssen: Phase I Trial of ARN-509 plus Abiraterone acetate, Docetaxel, and Prednisone in Patients with Metastatic Castrate Resistant Prostate Cancer (mCRPC) (c15-163) -PI Ana Molina M.D.

Subtask 4. Participate in > 6 trials initiated by other sites over 3 years.

We have opened 6 trials since the beginning of this award initiated by other sites.

Study Title
Northwestern: (BRCAAway) A Randomized Phase II Trial of Abiraterone, Olaparib, or Abiraterone + Olaparib in Patients with Metastatic Castration-Resistant Prostate Cancer with DNA Repair Defects [c16-168]
Duke: (STARTAR) A Salvage Trial of AR Inhibition with ADT and Apalutamide with Radiation therapy followed by Docetaxel in Men with PSA Recurrent Prostate Cancer after Radical Prostatectomy[c16-180]
MSKCC: (DORA) Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 for Metastatic Castration-Resistant Prostate Cancer (mCRPC) [c16-174]
University of Wisconsin: (IMMU Prostate) A Single-arm, Phase 2 Study to Evaluate the Safety and Efficacy of IMMU-132 in Patients with Metastatic Castration-Resistant Prostate Cancer Who Have Progressed on Second Generation AR-Directed Therapy [c18-204]
IRONMAN: Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (c16-170)
JHU TRIUMPH: Phase II Trial of Rucaparib in Patients with Metastatic Hormone-Sensitive Prostate Cancer Harboring Germline DNA Repair Gene Mutations (TRIUMPH) c18-220

Subtask 5. Ensure timely submission of quality data

We continue to work closely with the coordinating center and other sites to ensure timely data entry and responses to any queries.

SOW Major Task 3: Full participation in the consortium as a member of the Clinical Consortium Committee/Scientific Oversight Committee

Subtask 1. Participate in ≥1 PCCTC committee: Dr. Nanus is a member of the Scientific Oversight Committee and Dr. Tagawa serves as an Alternate.

Subtask 2. Attend all face-to-face meetings of the PCCTC: Dr. Nanus, Dr. Tagawa and/or Dr. Drake have attended all face-to-face meetings of the PCCTC, including GU ASCO, the ASCO annual meeting and the PCF Annual Retreat. ASCO was virtual this past year due to the COVID-19 pandemic.

Subtask 3. Participate in scheduled consortium conference calls: Dr. Nanus and/or Dr. Tagawa and/or Dr. Drake have participated in all PCCTC scheduled consortium conference calls. WCM investigators presented on the conference call in July 2020 discussing a new trial.
Subtask 4. Participate in review meetings/evaluation by the External Advisory Board (EAB): Dr. Nanus and/or Dr. Tagawa have attended all EAB meetings this past year.
Subtask 5. Compliance with the operations manual of the Consortium: We have been compliant.

SOW Major Task 4: Propose clinical trials to Consortium

Subtask 1. Propose new therapeutic trial to Coordinating Center and other Consortium sites: See above (Major Task 2, Subtask 3).
Subtasks 2- thru 7. Subtasks 2 thru 7 are completed for each WCMC or CUMC initiated protocol. (Submission of protocol for scientific review; start up at additional sites; clinical trial initiation at WCMC and other collaborating sites; Screen, enroll, and treat subjects; ongoing communication with study sites; Ongoing communication with IRB, DSMB, FDA).

SOW Major Task 5: Interim data analysis

Data analysis is ongoing from multiple studies. Since the last annual update, data from additional closed prior studies have been reviewed and verified. Data has been shared with the respective PI centers for multiple trials, including A Salvage Trial of AR Inhibition with ADT and Apalutamide with Radiation therapy followed by Docetaxel in Men with PSA Recurrent Prostate Cancer after Radical Prostatectomy (STARTAR) [c16-180]; An Open-Label Study of Rovalpituzumab Tesirine in Subjects with Delta-Like Protein 3-Expressing Advanced Solid Tumors(SCRX001-006) [c18-228]; Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in mCRPC [c14-144]; A Phase Ib/II Randomised Study of BI 836845 + Enzalutamide versus Enzalutamide alone in mCRPC [c14-147]; and Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in mCRPC [c14-144]. Abstracts and presentations of interim data are listed in **Major Task 8.**

SOW Major Task 6: Open other Consortium sponsored Clinical Trials at WCMC

See above in Major Task 2 for details.

SOW Major Task 7: Clinical trial performance

See above in Major Task 2 for details.

SOW Major Task 8: Analysis and reporting of data

Subtask 1. Verification of data

Queries have been completed and site visits have occurred when requested.

Subtask 2. Analysis of data

Data analysis is ongoing.

Subtask 3. Reporting of data in abstract form

2020 GU ASCO

Lang, JM, Kyriakopoulos, C, Slovin, SF, Eickhoff JC, Dehm, S, Tagawa, ST. Single-arm, phase II study to evaluate the safety and efficacy of sacituzumab govitecan in patients with metastatic castration-resistant prostate cancer who have progressed on second generation AR-directed therapy. ASCO GU 2020; Abstract TPS251.

Graff, JN, Antonarakis ES, Hoimes CJ, Tagawa ST, Hwang C, Kilari, D, Ten Tije AJ, Omlin AG, McDermott RS, Vaishampayan UN, Elliott A, Wu H, Kim J, Schloss C, DeBono JS. Pembrolizumab (pembro) plus enzalutamide (enza) for enza-resistant metastatic castration-resistant prostate cancer (mCRPC): KEYNOTE-199 cohorts 4-5. ASCO GU 2020; Abstract 15.

Vlachostergios PJ, Goswami S, Niaz MJ, Thomas C, Christos PJ, Osborne J, Vallabhajosula S, Molina AM, Sternberg CN, Singh S, Tan A, Patel A, Nanus DM, Bander, NH, Tagawa ST. Patient-reported outcomes (PRO) from a phase I/II dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration-resistant prostate cancer (mCRPC). ASCO GU 2020; Abstract 45.

Tagawa ST, Osborne J, Niaz MJ, Vallabhajosula S, Vlachostergios PJ, Thomas C, Molina AM, Sternberg CN, Singh S, Fernandez E, Babich J, Nanus DM, Ballman KV Bander NH. Dose-escalation results of a phase I study of 225Ac-J591 for progressive metastatic castration resistant prostate cancer (mCRPC). ASCO GU 2020; Abstract 114

Armstrong AJ, Luo J, Anand M, Antonarakis ES, Nanus DM, Giannakakou P, Szmulewitz RZ, Danila DC, Healy P, Berry WR, Wenstrup R, Scher HI, Tagawa ST, George DJ, Halabi S. AR-V7 and prediction of benefit with taxane therapy: Final analysis of PROPHECY. ASCO GU 2020; Abstract 184

Brown LC, Halabi S, Schonhoft J, Luo J, Nanus DM, Giannakakou P, Szmulewitz RZ, Danila DC, Healy P, Anand M, Somarelli J, Scher HI, Wenstrup R, Berry WR, Tagawa ST, Antonarakis ES, George DJ, Armstrong AJ. Association of circulating tumor cell chromosomal instability with worse outcomes in men with mCRPC treated with abiraterone or enzalutamide. ASCO GU 2020; Abstract 183

Gupta S, Halabi S, Kemeny G, Anand M, Nanus DM, Giannakakou P, George DJ, Gregory S, Armstrong AJ. Circulating tumor cell (CTC) genomic signatures of hormone therapy resistance in men with metastatic castration-resistant prostate cancer (mCRPC). ASCO GU 2020; Abstract 147

2020 AACR Virtual Annual Meeting

Phase I dose-escalation study of prostate-specific membrane antigen (PSMA)-targeted alpha emitter

225Ac-J591 for progressive metastatic castration resistant prostate cancer (mCRPC). Scott T. Tagawa, Joseph Osborne, Charlene Thomas, Escarleth Fernandez, Muhammad J. Niaz, Shankar Vallabhajosula, Panagiotis Vlachostergios, Ana M. Molina, Cora Sternberg, Sharon Singh, Amie Patel, Angela Tan, John Babich, David M. Nanus, Karla Ballman and Neil H. Bander. Cancer Res August 13 2020 80 (16 Supplement)

Androgen receptor (AR) genomic alterations and clinical outcome with prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy. Michael Sun, Muhammad Niaz, Charlene Thomas, Ariel Schaap, Kristine Lacuna, Panagiotis Vlachostergios, Paul Christos, Ana M. Molina, David M. Nanus, Cora N. Sternberg, Joseph Osborne, Neil H. Bander and Scott T. Tagawa Cancer Res August 13 2020 80 (16 Supplement)

2020 ASCO Virtual Annual Meeting

Aaron Scott Mansfield, David S. Hong, Christine L. Hann, Anna F. Farago, Himisha Beltran, Saiama Naheed Waqar, Andrew Eugene Hendifar, Lowell Brian Anthony, Matthew H. Taylor, Alan Haruo Bryce, Scott T. Tagawa, Karl D. Lewis, Jiaxin Niu, Christine H. Chung, James M. Cleary, Michael Rossi, Carrianne Ludwig, Ricardo Valenzuela, Yan Luo, Rahul Raj Aggarwal. A phase I/II study of rovalpituzumab tesirine in delta-like 3-expressing, advanced solid tumors. Proc ASCO 2020

Scott T. Tagawa, Joseph Osborne, Escarleth Fernandez, Charlene Thomas, Muhammad Junaid Niaz, Amy Ciriaco, Shankar Vallabhajosula, Panagiotis J. Vlachostergios, Ana M. Molina, Cora N. Sternberg, Sharon Singh, John Babich, David M. Nanus, Karla V. Ballman, Neil Harrison Bander. Phase I dose-escalation study of PSMA-targeted alpha emitter 225Ac-J591 in men with metastatic castration-resistant prostate cancer (mCRPC). Proc ASCO 2020

Christopher J. Hoimes, Julie N Graff, Scott T. Tagawa, Clara Hwang, Deepak Kilari, A. J. Ten Tije, Aurelius Omlin, Raymond S. McDermott, Ulka N. Vaishampayan, Tony Elliott, Winald R. Gerritsen, Haiyan Wu, Jeri Kim, Charles Schloss, Johann S. De Bono, Emmanuel S. Antonarakis. KEYNOTE-199 cohorts (C) 4 and 5: Phase II study of pembrolizumab (pembro) plus enzalutamide (enza) for enza-resistant metastatic castration-resistant prostate cancer (mCRPC). Proc ASCO 2020

ESMO Virtual Annual Meeting 2020

S.T. Tagawa, J.R. Osborne, A. Hackett, M.J. Niaz, V. Cooley, P. Christos, P.J. Vlachostergios, C. Thomas, L. Gracey, H. Beltran, A.M. Molina, D.M. Nanus, J. Babich, S. Vallabhajosula, O. Sartor, K. Ballman, N.H. Bander. Preliminary results of a phase I/II dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration resistant prostate cancer.

Subtask 4. Manuscript submission

Several manuscripts were published in 2019 and 2020 that reported final data on PCCTC trials or correlative studies that we led or participated in as listed below. Additional publications are under review or in preparation.

2019

Armstrong AJ, Halabi S, Luo J, Nanus DM, Giannakakou P, Szmulewitz RZ, Danila DC, Healy P, Anand M, Rothwell CJ, Rasmussen J, Thornburg B, Berry WR, Wilder RS, Lu C, Chen Y, Silberstein JL, Kemeny G, Galletti G, Somarelli JA, Gupta S, Gregory SG, Scher HI, Dittamore R, Tagawa ST, Antonarakis ES, George DJ. Prospective Multicenter Validation of Androgen Receptor Splice Variant 7 and Hormone Therapy Resistance in High-Risk Castration-Resistant Prostate Cancer: The PROPHECY Study. J Clin Oncol 2019;37:1120-1129.

Beltran H, Oromendia C, Danila DC, Montgomery B, Hoimes C, Szmulewitz RZ, Vaishampayan U, Armstrong AJ, Stein M, Pinski J, Mosquera JM, Sailer V, Bareja R, Romanel A, Gumpeni N, Sboner A, Dardenne E, Puca L, Prandi D, Rubin MA, Scher HI. Aurora kinase A inhibitor alisertib for patients with castration resistant and neuroendocrine prostate cancer: efficacy and biomarkers. Clin Cancer Res. 2019;25:43-51.

Heath EI, Nanus DM, Slovin S, Strand C, Higano C, Simons VH, Johnson C, Kyriakopoulos E, Reichert ZR, Lory S, George DJ, Mucci LA, Marcus JD, Trendel JA, Bock CH. Prostate Cancer National Summit's Call to Action. Clin Genitourin Cancer 2019;17:161-168.

Puca L, Gavyert K, Sailer V, Conteduca V, Dardenne E, Sigouros M, Isse K, Kearney M, Vosoughi A, Fernandez L, Pan H, Motanagh S, Hess J, Donoghue AJ, Sboner A, Wang Y, Dittamore R, Rickman D, Nanus DM, Tagawa ST, Elemento O, Mosquera JM, Saunders L, Beltran H. Delta-like protein 3 expression and therapeutic targeting in neuroendocrine prostate cancer. Sci Transl Med. 2019;11(484)

Tagawa ST, Antonarakis ES, Gjyrezi A, Galletti G, Kim S, Worroll D, Stewart J, Zaher A, Szatrowski TP, Ballman KV, Kita K, Tasaki S, Bai Y, Portella L, Kirby BJ, Saad F, Eisenberger MA, Nanus DM, Giannakakou P. Expression of AR-V7 and ARv567es in circulating tumor cells correlates with outcomes to taxane therapy in men with metastatic prostate cancer treated in TAXYNERGY. Clin Cancer Res 2019;25:1880-1888.

Tagawa ST, Vallabhajosula S, Christos PJ, Jhanwar YS, Batra JS, Lam L, Osborne J, Beltran H, Molina AM, Goldsmith SJ, Bander NH, Nanus DM. Phase 1/2 study of fractionated dose lutetium-177-labeled anti-prostate-specific membrane antigen monoclonal antibody J591 (177 Lu-J591) for metastatic castration-resistant prostate cancer. Cancer 2019;125:2561-569.

2020

Aggarwal RR, Schweizer MT, Nanus DM, Pantuck AJ, Heath EI, Campeau E, Attwell S, Norek K, Snyder M, Bauman L, Lakhotia S, Feng FY, Small EJ, Abida W, Alumkal JJ. A Phase Ib/IIa Study of the Pan-BET Inhibitor ZEN-3694 in Combination with Enzalutamide in Patients with Metastatic Castration-resistant Prostate Cancer. Clin Cancer Res. 2020;26(20):5338-5347.

Beltran H, Romanel A, Conteduca V, Casiraghi N, Sigouros M, Franceschini GM, Orlando F, Fedrizzi T,

Ku SY, Dann E, Alonso A, Mosquera JM, Sboner A, Xiang J, Elemento O, Nanus DM, Tagawa ST, Benelli M, Demichelis F. Circulating tumor DNA profile recognizes transformation to castration-resistant neuroendocrine prostate cancer. J Clin Invest 2020;130:1653-1668.

Gupta S, Hovelson DH, Kemeny G, Halabi S, Foo WC, Anand M, Somarelli JA, Tomlins SA, Antonarakis ES, Luo J, Dittamore RV, George DJ, Rothwell C, Nanus DM, Armstrong AJ, Gregory SG. Discordant and heterogeneous clinically relevant genomic alterations in circulating tumor cells vs plasma DNA from men with metastatic castration resistant prostate cancer. Genes Chromosomes Cancer. 2020;59(4):225-239.

Niaz MJ, Batra JS, Walsh RD, Vallabhajosula S, Jhanwar YS, Molina AM, Nanus DM, Osborne JR, Bander NH, Tagawa ST. Pilot study of hyperfractionated dosing of Lutetium-177-labeled antiprostate-specific membrane antigen monoclonal antibody J591 (177 Lu-J591) for metastatic castration-resistant prostate cancer. Oncologist 2020;25:477-e895.

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

Dr. Nauseef Jones is being mentored by Drs. Nanus and Tagawa (WCM fellow). Dr. Nauseef was awarded an ASCO Conquer Cancer Foundation Young Investigator Award for the Consortium clinical trial "An Open Label, Non-Randomized Phase II Trial of Cabozantinib in Patients with Metastatic CRPC and Known Amplifications or Activating Mutations in Gene Targets of Cabozantinib" which he wrote with Dr. Nanus. He was also accepted to the ASCO/AACR Methods in Clinical Cancer Research which was held virtually in an abbreviated fashion due to the Coronavirus pandemic.

Dr. Matthew Dallos (CUMC junior faculty) was being mentored by Dr. Charles Drake and is currently mentored by Dr. Mark Stein. Dr. Peter Gregos (junior WCM faculty at NYPBMH) is being mentored by Dr. Nanus.

How were the results disseminated to communities of interest?

Press releases from WCMC have accompanied publications of our data.

The WCM GU Oncology Program informs professional and the public via digital and social media channels (Facebook page (facebook.com/WeillCornellGUCancer); Twitter handle (twitter.com/cornellGUcancer); and online website (weillcornell.org/gucancer) and blog (weillcornellgucancer.org).

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

We will open additional PCCTC clinical trials at NYP Brooklyn Methodist Hospital. A new building with a dedicated oncology outpatient facility will open in Brooklyn in January 2020 which will increase patient referrals. We are currently interviewing for a patient navigator in Brooklyn to interact with the community, identify potential prostate cancer patients for clinical trials, and to assist patient enrolled on studies in remaining on trial and complying with the studies.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
Our 177Lu-PSMA-617 study has helped further define the appropriate dose for this agent, and our PSMA therapeutic program has helped define the role of PSMA therapy in patients with castrate resistant prostate cancer. Our randomized trial of Nivolumab or Nivolumab plus BMS-986253 is understand the role of immunotherapy in early stage prostate cancer. Our ARV7 study done in collaboration has prospectively identified ARV7 as a valid marker to predict resistance to second line anti-androgens.

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:

Dr. Panagiotis Vlachostergios who became a co-investigator on this award and was the lead at NYP Brooklyn Methodist Hospital had to return to Greece for personal family reasons. He has been replaced by Dr. Peter Gregos at NYP Brooklyn Methodist Hospital but Dr. Gregos will not as yet be a co-investigator on the grant.

Dr. Charles Drake left CUMC for industry in August 2020, although he continues to have an academic appointment at CUMC and will collaborate on immunology trials when appropriate. Dr. Mark Stein has become PI of the CUMC campus. Dr. Stein has previously served as an PCCTC investigator at the Rutgers Cancer Institute of New Jersey.

The COVID-19 pandemic has had a significant impact on patient accrual to clinical trials beginning in March 2020. At WCM and CUMC, research capabilities were on a day by day operations basis starting on March 10, 2020. All research enrollment and non-essential in person clinic visits were suspended by the Dean of Research and the institution on March 18, 2020. Clinical studies were not reopen to June and July on a rolling basis. Other aspects of clinical research were also affected, including protocol submission to the PRMC and IRB, and contract negotiations. Clinical trial accrual increased in August and September, but clinical volumes remain at approximately 80% of pre-COVID.

6. PRODUCTS:

See SOW Major Task 8, subtask 4

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Personnel	Role	Person Month	Percent Effort
David Nanus, M.D.	Principal Investigator	1.44	12%
Scott Tagawa, M.D.	Co-Investigator	1.44	12%
Sharon Singh	Clinical Research	6.0	50%
Mark Stein, M.D.	Principal Investigator	0.60	5%
Emerson Lim, M.D.	Collaborator	As needed	
Karla Ballman, M.D.	Collaborator	0.10	.08%
Jones Nauseef, M.D., Ph.D.	Postdoctoral fellow	1.0	8.33%
Peter Gregos, M.D.	Junior Faculty	1.0	8.33%
Matthew Dallos, M.D.	Junior Faculty	1.0	8.33%

Name: David M. Nanus, MD
Project Role: PI
Researcher Identifier: Orcid ID 0000-0003-3514-2976
Nearest person month worked: 1.44
Contribution to Project: Dr. Nanus has overseen the entire program, including organizing bi-weekly meetings, reviewing enrollment, meeting with WCM data coordinators and administrative staff, developing new protocols, and enrolling patients on studies.

Name: Scott Tagawa, MD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.44
Contribution to Project: Dr. Tagawa assists Dr. Nanus in coordinating and supervising all clinical research studies. He identifies and recruit patients to PCCTC clinical and translational research studies. He attends all PCTCC meetings.

Name: Mark Stein, MD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.6
Contribution to Project: Dr. Stein leads the CUMC effort, opening PCCTC trials at CUMC and managing the CUMC team involved. Dr. Stein also identifies and recruits patients to PCCTC clinical and translational research studies. He attends all PCTCC meetings.

Name: Sharon Singh
Project Role: Clinical Research Coordinator (WCM)
Researcher Identifier (e.g. ORCID ID):

Nearest person month worked: 6.0
Contribution to Project: Ms. Singh reports directly to Dr. Nanus and Dr. Tagawa. She guides clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.

Name: Karla Ballman, MD
Project Role: Collaborator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.1
Contribution to Project: Dr. Ballman assists with biostatistical design of WCM investigator initiated studies.

Name: Emerson Lim, MD
Project Role: Collaborator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: As needed
Contribution to Project: Dr. Lim identifies and recruit patients to PCCTC clinical and translational research studies.

Name: Matthew Dallos, MD
Project Role: Junior Faculty
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Dr. Dallos has worked with Dr. Drake to develop and write the Magic 8 trial. He coordinates patients on that study including the correlative science. He also accrues patients to PCCTC studies. He will supervise all immunologic and relevant translational science correlates from patients on studies.

Name: Jones Nauseef, MD, PhD
Project Role: Postdoctoral fellow
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Dr. Nauseef has worked with Dr. Nanus to develop and write clinical trials submitted to the PCCTC. He assists in recruiting patients to PCCTC studies.

Name: Peter Gregos, MD
Project Role: Junior Faculty
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Dr. Gregos accrues patients to PCCTC studies at NYP Brooklyn Methodist Hospital.

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

the last reporting period?

Nothing to report

What other organizations were involved as partners?

This grant is for the PCCTC consortium, which is a collaboration between all consortium sites.

8. SPECIAL REPORTING REQUIREMENTS:

None

9. APPENDICES:

Copies of 2020 manuscripts (see Major Task 9).