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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, New York, NY

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David Nanus, M.D.

E-Mail: dnanus@med.cornell.edu

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The Prostate Cancer Research Program at Weill Cornell Medicine (WCM) and NewYork-Presbyterian (NYP) is an internationally recognized prostate cancer (PC) clinical and translational research program. In 2017, we were awarded a Specialized Programs of Research Excellence (SPORE) grant in PC, highlighting the depth and breadth of our research. Since joining the Prostate Cancer Clinical Trials Consortium (PCCTC) as a Clinical Research Site in 2014, WCM has brought multiple high-impact and innovative therapeutic and biomarker studies to the PCCTC; enrolled more than 100 patients on clinical trials including 56 this past year; collected, processed, and analyzed over 500 tumor biopsy specimens, circulating tumor cells, and plasma and serum samples in a regulatory-compliant manner; complied with consortium-developed quality assurance and quality control procedures; and led PC advocacy initiatives within the PCCTC. We are expanding our site to include NYP Brooklyn Methodist Hospital (NYPBMH) and Columbia University Medical Center (CUMC).

15. SUBJECT TERMS
None listed.

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TABLE OF CONTENTS

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

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:

101 patients have enrolled to 17 PCCTC protocols in this reporting period including 28 patients to the Ironman Registry. Total enrollment number for the PCCTC trials are below in the Table.

Study Title	
Phase II Trial of Rucaparib in Patients with Metastatic Hormone-Sensitive Prostate Cancer Harboring Germline DNA Repair Gene Mutations (TRIUMPH) c18-220	1
A Phase 1/2, open-label, dose escalation and cohort expansion clinical trial to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARV-110 in patients with metastatic castration-resistant prostate cancer [c19-244]	8
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 (c20-254)	1

A Phase 1b/2 Study of BXCL701, a Small Molecule Inhibitor of Dipeptidyl Peptidases (DPP), Administered in Combination with the Anti-Programmed Cell Death 1 (PD-1) Monoclonal Antibody Pembrolizumab (PEMBRO; Keytruda®) in Patients with mCRPC either Small Cell Neuroendocrine Prostate Cancer (SCNC; NEPC) or Adenocarcinoma Phenotype" c20-263	8
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]	11
A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors [c20-259]	8
Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive mCRPC [c17-199]	0
Phase I dose−escalation trial of 225Ac−J591 in patients with mCRPC [c18-218]	0
Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (IRONMAN)	28
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]	16
A Randomized Phase II Trial of Abiraterone, Olaparib, or Abiraterone + Olaparib in Patients with mCRPC with DNA Repair Defects [c16-168]	1
Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 for mCRPC (DORA) [c16-174]	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]	0
A Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Prostate Specific Membrane Antigen (PSMA) Half Life Extended (HLE) Bispecific T-cell Engager (BiTE) AMG 160 in Subjects With Metastatic Castration Resistant Prostate Cancer (mCRPC) [c21-284]	2
SAABR: Single Arm Phase II Study of Abiraterone + Atezolizumab + GnRH and Stereotactic Body Radiotherapy (SBRT) to the Prostate in Men with Newly Diagnosed Hormone-sensitive Metastatic Prostate Cancer[c18-226]	4
A Multicenter, Open-Label, Parallel, Phase 1b/2a Study of PLX2853 in Combination with Abiraterone Acetate and Prednisone and Phase 1b/2a Study of PLX2853 in Combination with Olaparib in Subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) [c21-283]	8
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 [c21-276]	2

Total:	101

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

The numbers of patients enrolled from disproportionately affected populations are listed in the table blow. In addition, 23 patients to date of the 101 enrolled were United States Veterans.

Demographic	African American	White NH	White H	Asian	Other / Unknown	Total Subjects in Year
Year 3 10/1/20-9/30/21	17	64	8	1	11	101
	17%	63%	8%	1%	10%	

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 principal investigator (listed below).

- 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]
- 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 (c20-254)
- IIT Actinium: Phase I dose−escalation trial of 225Ac−J591 in patients with metastatic castration−resistant prostate cancer [c18-218]
- IIT PSMA 617 Fractionated: Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration resistant prostate cancer [c17-199]
- 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)
- 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]
- 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 [c21-276]
- A phase 1 study evaluating the safety, tolerability, pharmacokinetics, and efficacy of prostate specific membrane antigen (PSMA) Half Life Extended (HLE) Bispecific T-cell Engager (BiTE) AMG 160 in subjects with metastatic castration resistant prostate cancer. [c21-284]
- A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors [c20-259]

Upcoming Protocols to Submit:

- 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.
- A Phase 1B Multiple Dose, Multiple-Arm, Parallel Assignment Study to Evaluate the Safety, Tolerability, and Preliminary Efficacy of XmAb®20717 Alone or in Combination with Chemotherapy or Targeted Therapies in Selected Subjects with Metastatic Castration Resistant Prostate Cancer – PI Mark Stein M.D
- A Phase 1 Study of ADXS-504, a Cancer Type Specific Immunotherapy, With Biochemically Recurrent Prostate Cancer – PI Mark Stein M.D [pending LOI submission]

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

Currently we have/are participating in the following other institution protocols:

- 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]
- A Phase 1/2, open-label, dose escalation and cohort expansion clinical trial to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARV-110 in patients with metastatic castration-resistant prostate cancer [c19-244]
- Phase II Trial of Rucaparib in Patients with Metastatic Hormone-Sensitive Prostate Cancer Harboring Germline DNA Repair Gene Mutations (TRIUMPH) [c18-220]
- BioXcel: BXCL701:A Phase 1b/2 Study of BXCL701, a Small Molecule Inhibitor of Dipeptidyl Peptidases (DPP), Administered in Combination with the Anti-Programmed Cell Death 1 (PD-1) Monoclonal Antibody Pembrolizumab (PEMBRO; Keytruda®) in Patients with mCRPC either Small Cell Neuroendocrine Prostate Cancer (SCNC; NEPC) or Adenocarcinoma Phenotype [c20-263]
- UWash_SCCA_JNJ-63898081 PI Stein Full Title: A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors [c20-259]

- A Multicenter, Open-Label, Parallel, Phase 1b/2a Study of PLX2853 in Combination with Abiraterone Acetate and Prednisone and Phase 1b/2a Study of PLX2853 in Combination with Olaparib in Subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) [c21-283]
- A Phase 1/2 Feasibility, Safety, And Activity Study of PSCA-Specific Chimeric Antigen Receptor Engineered T Cells (BPX-601) In Subjects with Previously Treated Advanced Solid Tumors [c21-279]
- SAABR: Single Arm Phase II Study of Abiraterone + Atezolizumab + GnRH and Stereotactic Body Radiotherapy (SBRT) to the Prostate in Men with Newly Diagnosed Hormone-sensitive Metastatic Prostate Cancer [c18-226]
- A Phase 1/2, open-label, dose escalation and cohort expansion clinical trial to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARV-110 in patients with metastatic castration-resistant prostate cancer [c19-244]

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. Stein have attended all face-to-face (or virtual Zoom due to the COVID-19 pandemic) meetings of the PCCTC, including GU ASCO, the ASCO annual meeting and the PCF Annual Retreat.

Subtask 3. Participate in scheduled consortium conference calls: Dr. Nanus and/or Dr. Tagawa and/or Dr. Stein have participated in all PCCTC scheduled consortium conference calls.

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). In addition, the entire WCM PCCTC team together with CUMC have a bi-weekly phone calls at 8 AM on Thursday mornings.

SOW Major Task 5: Interim data analysis

Data analysis is ongoing from multiple studies. Since the last annual update, data from studies closed to accrual have been reviewed and verified. Data has been shared with the respective PI centers for multiple trials. 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

2021 GU ASCO

Jones T. Nauseef, Paul J. Christos, Charlene Thomas, Luke T. Nordquist, Cora N. Sternberg, Himisha Beltran, Sabrina Guervil, Giuseppe Galletti, Paraskevi Giannakakou, David M. Nanus, Scott T. Tagawa, Ana M. Molina. Phase I trial of apalutamide (Apa) with abiraterone acetate (AA) plus prednisone (P) and docetaxel (Doce) in patients with metastatic castration-resistant prostate cancer (mCRPC).

Michael Sun, Justin M Lebenthal, Jones T. Nauseef, Muhammad Junaid Niaz, Sabrina Guervil, Escarleth Fernandez, Amie Patel, Angela Tan, Panagiotis J. Vlachostergios, Joseph Osborne, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Neil Harrison Bander, Scott T. Tagawa. Baseline and post-treatment circulating tumor cell (CTC) counts with prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy (TRT) in men with metastatic castration-resistant prostate cancer (mCRPC).

Michael Sun, Jones T. Nauseef, Justin M Lebenthal, Muhammad Junaid Niaz, Sharon Singh, Tessa A Chamberlain, Mahelia Bissassar, Amie Patel, Angela Tan, Shankar Vallabhajosula, John Babich, Paul J. Christos, Joseph Osborne, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Neil Harrison Bander,

Scott T. Tagawa. A phase I/II dose-escalation study of fractionated and multiple dose 225Ac-J591 for progressive metastatic castration-resistant prostate cancer (mCRPC).

Howard I. Scher, Andrew J. Armstrong, Joseph D. Schonhoft, Audrey Gill, Jimmy Zhao, Ethan Barnett, Emily Carbone, James Lu, Emmanuel S. Antonarakis, Jun Luo, Scott T. Tagawa, Qian Yang, Daniel J. George, Russell Zelig Szmulewitz, Daniel Costin Danila, Rick Wenstrup, Mithat Gonen, Susan Halabi. Development and validation of circulating tumor cell (Epic Sciences) enumeration as a prognostic biomarker in men with metastatic castration-resistant prostate cancer.

2021 ASCO Virtual Annual Meeting

Scott T. Tagawa, Michael Sun, A. Oliver Sartor, Charlene Thomas, Sharon Singh, Mahelia Bissassar, Escarleth Fernandez, Muhammad Junaid Niaz, Benedict Ho, Shankar Vallabhajosula, John Babich, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Joseph Osborne, Neil Harrison Bander. Phase I study of 225Ac-J591 for men with metastatic castration-resistant prostate cancer (mCRPC).

Johann S. De Bono, Lawrence Fong, Tomasz M. Beer, Xin Gao, Daniel M. Geynisman, Howard A. Burris III, James Fredric Strauss, Kevin Dale Courtney, David I. Quinn, David James VanderWeele, Yifah Yaron, Che-Leung Law, Mark N. Stein. Results of an ongoing phase 1/2a dose escalation study of HPN424, a tri-specific half-life extended PSMA-targeting T-cell engager, in patients with metastatic castration-resistant prostate cancer (mCRPC).

Michael J. Morris, Ronald De Wit, Nicholas J. Vogelzang, Scott T. Tagawa, Celestia S. Higano, Paul Hamberg. A phase III trial of docetaxel versus docetaxel and radium-223 (Ra-223) in patients with metastatic castration-resistant prostate cancer (mCRPC): DORA.

Julie N Graff, Scott T. Tagawa, Christopher J. Hoimes, Winald R. Gerritsen, Ulka N. Vaishampayan, Tony Elliott, Clara Hwang, A. J. Ten Tije, Aurelius Omlin, Raymond S. McDermott, Yves Fradet, Deepak Kilari, Cristiano Ferrario, Hiroji Uemura, Cuizhen Niu, Christian Heinrich Poehlein, Ronald De Wit, Charles Schloss, Johann S. De Bono, Emmanuel S. Antonarakis. Pembrolizumab plus enzalutamide for enzalutamide-resistant metastatic castration-resistant prostate cancer (mCRPC): Updated analyses after one additional year of follow-up from cohorts 4 and 5 of the KEYNOTE-199 study.

Michael Sun, Charlene Thomas, Benedict Ho, Muhammad Junaid Niaz, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Neil Harrison Bander, Scott T. Tagawa. Long-term adverse events (AE) in patients with metastatic castration-resistant prostate cancer (mCRPC) receiving prostate-specific membrane antigen (PSMA)-based targeted radionuclide therapy (TRT).

Jones T. Nauseef, Sharon Singh, Angela Tan, Amie Patel, Brian D. Robinson, Francesca Khani, Charles G. Drake, Emerson A. Lim, Mark N. Stein, Elisabeth I. Heath, Himisha Beltran, Ana M. Molina, Bishoy Morris Faltas, Karla V. Ballman, Cora N. Sternberg, Scott T. Tagawa, David M. Nanus. Open label phase II trial of cabozantinib (cabo) in patients with metastatic castrate resistant prostate cancer (mCRPC) and known amplifications or activating mutations in gene targets who have received prior anti-androgen therapy.

ESMO Virtual Annual Meeting 2021

Brian D. Gonzalez, Michael Sun, Charlene Thomas, Sarah L. Eisel, Laura B. Oswald, Heather S. L. Jim, Benedict Ho, Amie Patel, Angela Tan, Muhammad J. Niaz, Cora N. Sternberg, Ana Molina, David Nanus, Joseph Osborne, Neil Bander, Scott T. Tagawa. Patient-Reported Outcomes in Prostate Cancer Patients Receiving PSMA-Targeted Radionuclide Therapy.

Scott T. Tagawa, Michael Sun, A. Oliver Sartor, Charlene Thomas, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Neil H. Bander. Final results of phase I/II trial of fractionated dose 177Lu-PSMA-617 for metastatic castration-resistant prostate cancer (mCRPC).

J.N. Graff, S. Tagawa, C. Hoimes, W. Gerritsen, U.N. Vaishampayan, T. Elliott, C. Hwang, A.J. Ten Tije, A.G. Omlin, R.S. McDermott, R. De Wit, P. Qiu, C. Poehlein, J. Kim, L. Suttner, R. Cristescu, M.J. Marton, C. Schloss, J.S. de Bono, E.S. Antonarakis. Biomarker analysis of men with enzalutamide (enza)-resistant metastatic castration-resistant prostate cancer (mCRPC) treated with pembrolizumab (pembro) + enza in KEYNOTE-199.

Paul Monk III, Jingsong Zhang H. Lee, Mark Linch, Scott Tagawa, Dan Costin, Daniel Peter Petrylak, Lawrence Karsh, Rob Jones, Xinhua Zhu, Veena Agarwal, Pascal Borderies, Rashmi Deshpande, Vince O'Neill, Rahul Raj Aggarwal. BXCL701 - 1st-in-class oral activator of systemic innate immunity-combined with pembrolizumab, in men with metastatic castration-resistant prostate cancer (mCRPC): Phase II results.

2021 AUA Virtual Annual Meeting

Michael Sun, Charlene Thomas, Benedict Ho, Junaid Niaz, Jones Nauseef, Joseph Osborne, Ana Molina, Cora Sternberg, David Nanus, Neil Bander, and Scott Tagawa. Long-term follow-up and prognostic factor analysis in men with metastatic castration-resistant prostate cancer (mCRPC) who receive prostate-specific membrane antigen (PSMA)-targeted lutetium-177 (177Lu).

Subtask 4. Manuscript submission

Several manuscripts have been published in 2019, 2020 and 2021 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

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Armstrong AJ, Luo J, Nanus DM, Giannakakou P, Szmulewitz RZ, Danila DC, Healy P, Anand M, Berry WR, Zhang T, Harrison MR, Lu C, Chen Y, Galletti G, Schonhoft JD, Scher HI, Wenstrup R, Tagawa ST, Antonarakis ES, George DJ, Halabi S. Prospective Multicenter Study of Circulating Tumor Cell AR-V7 and Taxane Versus Hormonal Treatment Outcomes in Metastatic Castration-Resistant Prostate Cancer. JCO Precis Oncol. 2020 Oct 28;4.

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2021

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

Dr. Nauseef Jones is being mentored by Drs. Nanus and Tagawa (WCM junior faculty). 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 opened in Brooklyn in January 2021 with a dedicated oncology floor. We hired a genitourinary nurse practitioner at NYPBMH to specifically work with Drs. Nanus and Gregos to care for men with prostate cancer, and to help enroll patients onto clinical trials. We have also submitted a grant which we anticipate funding to hire a prostate cancer patient navigator in Brooklyn. We have also engaged investigators at the James J. Peters Department of Veterans Affairs Medical Center in the Bronx, NY (affiliated with CUMC) and are in discussions to open additional PCCTC studies there (in addition to DORA which is currently open).

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 and schedule dose for this agent, which is planned to be included as a cohort in the phase III STAMPEDE study, 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 designed to better 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:

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.	Junior Faculty	1.0	8.33%
Peter Gregos, M.D.	Junior Faculty	1.0	8.33%
Matthew Dallos, M.D.	Junior Faculty	1.0	8.33%
Cora Sternberg, M.D.	Senior 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: Junior Faculty
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?

New Support:

Dr. David Nanus

Title: Novel complex structural variants and epigenetic alterations link the genomes of prostate cancer in African Americans with outcome disparity
Time Commitments: .06 calendar
Supporting Agency: U.S. Department of Defense W81XWH-20-PCRP-HDRA (Mosquera)
Address: 820 Chandler Street, Fort Detrick, MD 21702-5014
Contracting/Grants Officer:
Performance Period: 07/01/2021 – 06/30/2023
Level of funding:
Project Goals: The goal of this project is to identify and interrogate the underlying genetic differences that contribute to worse outcomes in men of African descent with prostate cancer. The project will develop a cohort of African American men with prostate, identify structural variants in chromosomes and epigenetic changes that contribute to disease progression, and correlate these findings with outcomes disparities.
Overlap: None

Dr. Scott Tagawa

W81XWH-18-PCRP-CTA PC190642 (Tagawa)
Heating Cold Prostate Tumors with PSMA-Targeted Alpha Therapy and Pembrolizumab
1.2 calendar
Department of Defense
Joshua D. McKean, Grant Specialist, 301-619-9656, e-mail:joshua.d.mckean3.civ@mail.mi
09/30/2020 – 08/31/2024
Goals: To assess efficacy and safety of ^{225}Ac-J591 with pembrolizumab and AR signaling inhibitor in patients with chemo-naïve metastatic castration-resistant prostate cancer.
Role: Principal Investigator

W81XWH-19-PCRP-IDA (Gonzalez)
Measuring Patient-Reported Outcomes Related to Radiopharmaceuticals for Prostate Cancer
To create a new patient-reported outcomes measure for patients receiving targeted radionuclide therapy
0.6 calendar
Department of Defense
09/01/2020-08/31/2023
Goals to create a new patient-reported outcomes measure for patients receiving targeted radionuclide therapy
Role: Co-Investigator

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 2021 manuscripts (see Major Task 9).