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TITLE: Targeted Therapies

PRINCIPAL INVESTIGATOR: Dr. Scott Tagawa, MD, MS

CONTRACTING ORGANIZATION: Joan and Sanford I Weill Medical College of Cornell University

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The objective of this research is for WCM, together with NYP Brooklyn Methodist Hospital (BMH) and Columbia University Medical Center (CUMC), to participate in the PCCTC as a multisite Clinical Research Site. Our overall aim is to translate our prostate cancer (PC) 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 and veterans.

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 NYP Brooklyn Methodist Hospital (BMH) and Columbia University Medical Center (CUMC), to participate in the PCCTC as a multisite Clinical Research Site. Our overall aim is to translate our prostate cancer (PC) 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 and veterans. 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?

Major Task 1: Completion of regulatory review, Clinical Trial Startup

Subtask 1: Initiate and complete contractual agreements between PCCTC LLC with VAMC:
This has been completed.

Subtasks 2 – 4: (Submission of protocols for scientific Protocol Review and IRB Submission; Clinical trial approval; Site initiation visits (CUMC and BMH)):
This is ongoing. See Major Task 2, Subtask 3 for details on pending studies in regulatory review and start-up process.

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

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

Summary: There were 17 PCCTC protocols that were open during this reporting period of **October 1st, 2022 – September 30, 2023** (including 13 open to enrollment and 4 currently closed to enrolment trials). Total enrollment numbers are shown in the table below.

Full Study Title [PCCTC #]	**Sites OTE during this period**	**# Screened Total (entire lifespan)**	**# Enrolled Total (entire lifespan)**	**# Enrolled during this annual reporting period**
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]	WCM	16	6	WCM: 1
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]	WCM	6	6	WCM: 0
A Phase 1, Multicenter, Open-label, Dose-escalation, and Dose-expansion Study to Evaluate the Safety, Pharmacokinetics, and Anti-tumor Activity of ARX517 in Subjects with Advanced Solid Tumors Who Failed Prior Standard Therapies [c23-326]	WCM	14	11	WCM: 11*
A Phase 1b Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of Delta-like Protein 3 Half-life Extended Bispecific T-cell Engager AMG 757 in Subjects with De Novo or Treatment Emergent Neuroendocrine Prostate Cancer [c21-273] *(On Enrollment Hold)*	WCM	2	0	WCM: 0
A Phase 1b/2 Study of BXCL701, a Small Molecule Inhibitor of Dipeptidyl Peptidases (DPP), Administered in Combination with	WCM	16	13	WCM: 1

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] *(Closed to Enrollment)*				
ZEN003694-201: Randomized Phase 2b Study of ZEN003694 in Combination with Enzalutamide versus Enzalutamide Monotherapy in Patients with Metastatic Castration-Resistant Prostate Cancer [c22-298] *(Closed to Enrollment)*	WCM	1	1	WCM: 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] *(Closed to Enrollment)*	WCM	14	12	WCM: 1
Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 for Metastatic Castration-Resistant Prostate Cancer (mCRPC) (DORA) [c16-174]	WCM, BMH	13	8	WCM: 4 BMH: 0
Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (IRONMAN) [c16-170]	WCM, BMH, CUMC	143	137	22
Phase I/II trial of pembrolizumab and androgen-receptor pathway inhibitor with or without 225Ac-J591 for progressive metastatic castration resistant prostate cancer [c23-336]	WCM, BMH, CUMC (pending activation)	25	22	WCM: 22* BMH: 0
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	WCM, CUMC	26	23	WCM: 18 CUMC: 2

Randomized Control Trial [c22-301]				
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]	WCM, CUMC	2	2	WCM: 1 CUMC: 0
A Phase 1/Phase 2 Trial to Evaluate Safety, Immunogenicity and PSA Response of VTP-850 Prostate Cancer Immunotherapeutic in Men with Biochemical Recurrence after Definitive Local Therapy for Prostate Cancer [c21-295]	CUMC	2	1	CUMC: 1
A Phase 1 Study of JNJ-78278343, a T-Cell-Redirecting Agent Targeting Human Kallikrein 2 (KLK2), for Advanced Prostate Cancer [c22-297]	CUMC	16	16	CUMC: 10
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 (Xencor) [c20-250]	CUMC	7	6	CUMC: 2
A Phase I, Multi-Center, Open-Label, Dose-Finding Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of CC-94676 in Subjects with Metastatic Castration-resistant Prostate Cancer [c20-255]	CUMC	2	2	CUMC: 2
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 (SAABR) [c18-226] *(Closed to Enrollment)*	CUMC	3	3	CUMC: 0

* Number represents total enrolment since study activation since this study was recently added to the PCCTC portfolio and thus previously was not reported

Note:
Enrolment definition: Undergone screening and have begun/completed study procedures (Excluding screen failures). Included here if date of consent/screening process initiation was within the reporting period.

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

25 of 99 patients (25%) were from disproportionately affected populations. In addition, 16 patients out of the 99 (16%) patients were United States Veterans.

	Demographics					
	African American	**White Hispanic**	**White Non-Hispanic**	**Asian**	**Other/ Unknown**	**Total Subjects**
10/1/2022-9/30/2023	17	8	70	1	3	99
	17%	8%	71%	1%	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 previously opened the following clinical trials for which WCMC serves as lead site:

- 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] – PI: David Nanus, M.D.
- 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] – PI: Scott Tagawa, M.D.
- 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] – PI: Scott Tagawa, M.D.
- A Phase 1b Open-Label, Clinical Trial to Evaluate the Safety, Tolerability, and Pharmacokinetics of ARV-110 in Combination with Abiraterone in Patients with Metastatic Prostate Cancer [c21-293] – PI: Cora Sternberg, M.D.
- 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 [c22-301] – PI: David Nanus, M.D.

- Phase I/II trial of pembrolizumab and androgen-receptor pathway inhibitor with or without 225Ac-J591 for progressive metastatic castration resistant prostate cancer [c23-336] – PI: Scott Tagawa, M.D.

Protocols that have been in regulatory/start-up process at sites during this reporting period:

- A Phase 1/2 Open-Label, Dose-Escalation and Cohort Expansion Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARV-766 in Patients with Metastatic Castration-Resistant Prostate Cancer [c22-302] - Pending start-up at WCM
- Phase I/II of pembrolizumab and androgen-receptor pathway inhibitor with or without 225Ac-J591 for progressive metastatic castration resistant prostate cancer – Pending start-up at CUMC
- A Phase 1/Phase 2 Trial to Evaluate Safety, Immunogenicity and PSA Response of VTP-850 Prostate Cancer Immunotherapeutic in Men with Biochemical Recurrence after Definitive Local Therapy for Prostate Cancer [c21-295] – Pending start-up at WCM
- A Phase 1/2 study of MCG018 in Combination with MGD019 in Participants with Advanced Solid Tumors (CP-MGC018-02; Macrogenics) [c23-318] – Pending start-up at WCM

Subtask 4: Participate in > 6 trials initiated by other sites (site leads) over 3 years:

We are currently participating in the following protocols initiated by other institutions other than WCM (including both open and closed to enrollment studies):

- Northwestern: A Randomized Phase II Trial of Abiraterone, Olaparib, or Abiraterone + Olaparib in Patients with Metastatic Castration-Resistant Prostate Cancer with DNA Repair Defects (BRCAAway) [c16-168] – WCM PI: Scott Tagawa, M.D.
- IRONMAN (Duke, MSK, DFCI): Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer [c16-170] – WCM/CUMC PIs: Scott Tagawa, M.D. and Mark Stein, M.D.
- MSK: Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 for Metastatic Castration-Resistant Prostate Cancer (mCRPC) (DORA) [c16-174] – WCM PI: Scott Tagawa, M.D.
- Duke: 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] -WCM PI: Scott Tagawa, M.D.
- University of Wisconsin: 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 (IMMU Prostate) [c18-204] – WCM PI: Scott Tagawa, M.D.
- JHU: Phase II Trial of Rucaparib in Patients with Metastatic Hormone-Sensitive Prostate Cancer Harboring Germline DNA Repair Gene Mutations (TRIUMPH) [c18-220] – WCM PI: Cora Sternberg, M.D.
- MSK, Columbia: 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 (SAABR) [c18-226]- CUMC PI: Karie Runcie, M.D.

- Columbia: 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] – CUMC PI: Mark Stein, M.D.
- Columbia: 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 [c20-250] – CUMC PI: Mark Stein, M.D.
- MSK: A Phase 1, Multi-Center, Open-Label, Dose Finding Study to Evaluate the Safety, Tolerability, Pharmacokinetics, And Pharmacodynamics of CC-94676 In Subjects with Metastatic Castration-Resistant Prostate Cancer [c20-255] – CUMC PI: Karie Runcie, M.D.
- University of Washington: A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors [c20-259] – CUMC PI: Mark Stein, M.D.
- UCSF: 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]
- UCSF: A Phase 1b Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of Delta-like Protein 3 Half-life Extended Bispecific T-cell Engager AMG 757 in Subjects with De Novo or Treatment Emergent Neuroendocrine Prostate Cancer [c21-273]– WCM PI Dr. Cora Sternberg, MD
- KCC: 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] – CUMC PI: Mark Stein, M.D.
- University of Chicago: 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] – CUMC PI: Mark Stein, M.D.
- Columbia, University of Washington: A Phase 1 Study of JNJ-78278343, a T-Cell-Redirecting Agent Targeting Human Kallikrein 2 (KLK2), for Advanced Prostate Cancer [c22-297] – CUMC PI: Mark Stein, M.D.
- University of Michigan, UCSD: Randomized Phase 2b Study of ZEN003694 in Combination with Enzalutamide versus Enzalutamide Monotherapy in Patients with Metastatic Castration-Resistant Prostate Cancer [c22-298] – WCM PI: David Nanus M.D.

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.

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. Tagawa is a member of the Scientific Oversight Committee and Prostate Cancer Working Group 4.

Subtask 2: Attend all face-to-face meetings of the PCCTC**:**
Dr. Tagawa, Dr. Nanus 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. Tagawa and/or Dr. Nanus 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. Tagawa and/or Dr. Nanus have attended all EAB meetings this past year.

Subtask 5: Compliance with the operations manual of the Consortium:
We have been compliant.

Major Task 4: Propose clinical trials to Consortium

Subtask 1: Propose new therapeutic trials to Coordinating Center and other Consortium sites:
See above (Major Task 2, Subtask 3) for details.

Subtasks 2 – 7:
Subtasks 2 through 7 are ongoing 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.

Major Task 5: Interim data analysis

Subtask 1: (Verification of data) and Subtask 2 (Compilation of data to DSMC for review):
Data analysis is ongoing for 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. Appropriate data have been compiled for DSMC review at given timelines. Abstracts and presentations of interim data are listed in Major Task 8.

Major Task 6: Open other Consortium sponsored Clinical Trials at WCMC
See above in Major Task 2 for details.

Major Task 7: Clinical trial performance
See above in Major Task 2 for details.

Major Task 8: Analysis and reporting of data

Subtasks 1 and 2: Verification of data and Analysis of data:
Queries have been completed and site visits have been conducted when necessary.
Data analysis of protocols is ongoing.

Subtask 3: Reporting of data in abstract form:

See below list of abstracts/presentations from this annual reporting period:

Michael Philip Sun, Jones T. Nauseef, Jessica Palmer, Joseph Earl Thomas, Judith Stangl-Kremser, Mahelia Bissassar, Sandra Huicochea Castellanos, Joseph Osborne, Ana M. Molina, Cora N. Sternberg, David M. Nanus, Neil Harrison Bander, and Scott T. Tagawa. Phase I results of a phase I/II study of pembrolizumab and AR signaling inhibitor (ARSI) with 225Ac-J591. Journal of Clinical Oncology 2023 41:6_suppl, 181-181

Mucci L, Vinson J, Gerke T, Hyslop T, Howard L, Dreicer R, Rathkopf D, Chi K, Esteban E, Enting D, Bjartell A, Tagawa S, Nanus D, Ong M, Barata P, Hotte S, Grant M, Villanti P, Kantoff P, George D. First look at the baseline characteristics of participants in IRONMAN, the international registry for men with advanced prostate cancer. J Clin Oncol 41, 2023 (suppl 6; abstr 85)

Tian Zhang, Lauren Howard, Bridget Koontz, Scott Tagawa, Himanshu Nagar, Rhonda Bitting, Bart Frizzell, Luke Nordquist, Julia Rasmussen, Carolyn Winters, Colleen Riggan, Marco Reyes-Martinez, Catrin Davies, Steven Gray, Carly Newman, Escarleth Fernandez, Michael Harrison, Daniel George, Yuan Wu, Andrew Armstrong. Primary analysis of STARTAR: A phase 2 salvage trial of androgen receptor (AR) inhibition with androgen deprivation therapy (ADT) and apalutamide with radiation therapy (RT) followed by docetaxel in men with PSA recurrent prostate cancer (PC) after radical prostatectomy (RP). J Clin Oncol 41, 2023 (suppl 16; abstr 5016)

Markowski M, Sternberg C, Wang H, Sullivan R, King S, Lotan T, Antonarakis E. TRIUMPH: Phase II trial of rucaparib monotherapy in patients with metastatic hormone-sensitive prostate cancer harboring germline DNA repair gene mutations. J Clin Oncol 41, 2023 (suppl 6; abstr 190)

Aggarwal R, Zhang J, Zhu X, Monk P, Jones R, Linch M, Costin D, De Bono J, Karsh L, Petrylak D, Borderies P, Deshpande R, Hafeez A, O'Neill V, Tagawa S. First-in-class oral innate immune activator BXCL701 combined with pembrolizumab in patients with metastatic, castration-resistant prostate cancer (mCRPC) of small cell neuroendocrine (SCNC) phenotype: Phase 2a final results. J Clin Oncol 41, 2023 (suppl 6; abstr 176)

Rahul Aggarwal, Jingsong Zhang, Paul Monk, Xinhua Zhu, Dan Costin, Daniel Petrylak, Pascal Borderies, Rashmi Deshpande, Amir Hafeez, Vincent O'Neill, Scott Tagawa. First-in-class oral innate immune activator BXCL701 combined with pembrolizumab, in patients with metastatic castration-resistant prostate cancer (mCRPC) of small cell neuroendocrine (SCNC) variant: Randomized phase 2b trial. J Clin Oncol 41, 2023 (suppl 16; abstr TPS5109)

Bryce A, Karp D, Tagawa S, Nordquist L, Rathkopf D, Adra N, Dorff T, Baeck J, O'Donnell J, Ames T, Yim C, Price M, Scher H. A phase 2 study of immunogenic cell death inducer PT-112

in patients with metastatic castration-resistant prostate cancer. J Clin Oncol 41, 2023 (suppl 6; abstr TPS292)

Nicole Jacobs, Katie Hootman, Victoria Fischer, Nadja Pinnavaia, Karen Sfanos, Jones Nauseef, Ana Molina, Cora Sternberg, Scott Tagawa, Karla Ballman, Mark Stein, Channing Paller, David Nanus. Whole-food plant-based diet (WFPBD) to control weight and metabo-inflammation in overweight/obese men with prostate cancer (PC) receiving androgen deprivation therapy (ADT): A multi-center randomized control trial. J Clin Oncol 41, 2023 (suppl 16; abstr TPS5098)

Mark Stein, Jessica Hawley, Russell Pachynski, Kevin Zarrabi, Robert Dreicer, Matthew Zibelman, Margaret Marshall, Bethan Jones, Vicky Wheeler, Sarah Sebastian, Jennifer Bendall, Katie Anderson, Neal Shore, Julie Graff. Prime-boost immunotherapeutic trial in men with biochemical recurrence after definitive local therapy for prostate cancer. J Clin Oncol 41, 2023 (suppl 16; abstr TPS5119)

Subtask 4: Manuscript submission:

Please see list below of publications from this reporting period. Additional publications are under review or in preparation.

Slovin SF, Knudsen K, Halabi S, de Leeuw R, Shafi A, Kang P, Wolf S, Luo B, Gopalan A, Curley T, Fleming M, Molina A, Fernandez C, Kelly K. Randomized Phase II Multicenter Trial of Abiraterone Acetate With or Without Cabazitaxel in the Treatment of Metastatic Castration-Resistant Prostate Cancer. J Clin Oncol. 2023 Aug 15:JCO2202639. doi: 10.1200/JCO.22.02639. Epub ahead of print.

Gupta S, Halabi S, Yang Q, Roy A, Tubbs A, Gore Y, George DJ, Nanus DM, Antonarakis ES, Danila DC, Szmulewitz RZ, Wenstrup R, Armstrong AJ. PSMA-positive circulating tumor cell detection and outcomes with abiraterone or enzalutamide treatment in men with metastatic castrate resistant prostate cancer. Clin Cancer Res. 2023 Mar 10:CCR-22-3233.

Rencsok EM, Slopen N, Autio K, Morgans A, McSwain L, Barata P, Cheng HH, Dreicer R, Heath E, McKay RR, Pomerantz M, Rathkopf D, Tagawa S, Whang YE, Ragin C, Odedina FT, George DJ, Kantoff PW, Vinson J, Villanti P, Haneuse S, Mucci LA; IRONMAN Registry. Quality of life in the year after new diagnosis with advanced prostate cancer for Black and White individuals living in the US. Qual Life Res. 2023 Jul 6. doi: 10.1007/s11136-023-03468-0. Epub ahead of print.

What opportunities for training and professional development has the project provided?
Dr. Jones Nauseef is being mentored by Drs. Nanus and Tagawa (WCM junior faculty).
Dr. Peter Gregos (junior WCM faculty at NYPBMH) is being mentored by Dr. Nanus.
Dr. Alexander Wei is being mentored by Dr. Mark Stein, at CUMC.

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/WCMGUcancer); 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?

Broadening the participation to Bronx VA Medical Center to increase underrepresented minority group and Veteran participation in these studies. More detailed information and accrual numbers on studies from this site will be included in the next report.

4. IMPACT:

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

The 177Lu-PSMA-617 study contributed to the approval of the drug (Pluvicto). The Phase 1 Actinium study results have led to development of 2 new trials that have been recently added to this Consortium ("Phase I/II trial of pembrolizumab and androgen-receptor pathway inhibitor with or without 225Ac-J591 for progressive metastatic castration resistant prostate cancer" and "A Phase 1, Multicenter, Open-label, Dose-escalation, and Dose-expansion Study to Evaluate the Safety, Pharmacokinetics, and Anti-tumor Activity of ARX517 in Subjects with Advanced Solid Tumors Who Failed Prior Standard Therapies"). These trials will continue to advance our understanding of the role of PSMA therapy in patients with metastatic castration-resistant prostate cancer.

What was the impact on other disciplines?
The research work on radionuclides in these studies have led to revelations across other tumor types and have provided information for continuing research in other tumor types.

What was the impact on technology transfer?
There was a patent application titled "Radiotherapeutic Conjugates for Treating Cancer" for technology transfer.

What was the impact on society beyond science and technology?
Nothing to Report.

5. CHANGES/PROBLEMS:

The accruing issues that stemmed from the COVID-19 pandemic have improved, as we were able to hire new personnel and accrue an adequate number of subjects into PCCTC trials. Furthermore, new PCCTC trials are in regulatory start-up. However, 75% of the clinical research team at WCM GU Oncology are new to their roles within the past year, so there is great potential to increase accrual and start-up timelines within the next year as personnel become fully acclimated to their roles.

The issue with delayed reports has improved since the last annual and semi-annual reporting period, with the additional GU Clinical Trials Administrator on the team, however there is still progress to be made to submit all reports prior to the deadline.

6. PRODUCTS:

Please see Major Task 8 above for details.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Personnel	Role	Person Month Effort	Percent Effort
Scott Tagawa	PD/PI	1.8 CM	15%
David Nanus	Co-Investigator	1.2 CM	10%
Devan-Ann Louissaint	Clinical Research Specialist	1.33 CM	11.15%
Sarah Yuan	Clinical Trials Administrator	8.65 CM	72.1%
May Ann Todd	Clinical Research Assistant	6.43 CM	53.56%

Name: Scott Tagawa, MD
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.8
Contribution to Project: Dr. Tagawa 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: David M. Nanus, MD
Project Role: Co-Investigator
Researcher Identifier: Orcid ID 0000-0003-3514-2976
Nearest person month worked: 1.2
Contribution to Project: Dr. Nanus is involved with coordinating and supervising all clinical research studies, meeting with WCM data coordinators and administrative staff, developing new protocols, and enrolling patients on studies. He identifies and recruit patients to PCCTC clinical and translational research studies. He attends all PCTCC meetings.

Name: Devan-Ann Louissaint
Project Role: Clinical Research Specialist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.33
Contribution to Project: Ms. Louissaint reports directly to Dr. Tagawa and Dr. Nanus. She guides clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.

Name: Sarah Yuan
Project Role: Clinical Trials Administrator

Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 8.65
Contribution to Project: Ms. Yuan reports directly to Dr. Tagawa and Dr. Nanus. She guides clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.

Name: May Ann Todd
Project Role: Clinical Research Assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6.43
Contribution to Project: Ms. Todd reports directly to Dr. Tagawa and Dr. Nanus. She assists with data entry and query resolution for studies.

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

Please see above Section 7 for details on personnel at WCM who were associated with this grant.

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

Nothing to Report.

9. APPENDICES:

Nothing to Report.