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14. ABSTRACT
Purpose: The purpose of the PCCTC is to accelerate the development of novel therapeutics for prostate cancer patients, both by bringing own areas of expertise and contributing substantially to the activity of the consortium in the areas of biomarker development, androgen receptor targeted therapies, aggressive variant/neuroendocrine prostate cancer, and theranostics/novel molecular imaging.
Results: During the overall grant period, 163 patients were enrolled across PCCTC clinical trials, including ten trials led or co-led by UCSF.

15. SUBJECT TERMS
Prostate cancer, Phase 1, Phase 2, clinical consortium, infrastructure, collaboration

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1. Introduction

As a Clinical Research Site of the Department of Defense Prostate Cancer Clinical Trials Consortium (PCCTC), UCSF's ultimate goal is to continue the accelerated development of novel therapeutics for prostate cancer patients, both by bringing our own areas of expertise to the consortium, while also contributing substantially to the activity of the PCCTC. UCSF is ideally situated to continue to serve as a productive and creative participant in the PCCTC, by virtue of 1) the integration and interaction of outstanding basic, translational, and clinical research programs led by national and international opinion leaders, 2) a robust and mature research infrastructure, 3) significant institutional commitment to this research, 4) extensive experience in conducting clinical trials, 4) a strong pipeline of novel agents, and 5) extensive collaborations in many multi-center clinical trial programs.

2. Keywords

Prostate cancer, Phase I, Phase II, clinical consortium, infrastructure, collaboration

3. Accomplishments

What were the major goals of the project?

The major goals of the project as stated in the approved SOW include the following:

1) Adhere to performance metrics defined by Coordinating Center

2) Full participation in the consortium as a member of the Clinical Consortium Committee/ Scientific Oversight Committee

3) Leverage the integration of PCCTC clinical trials into tumor and DNA acquisition strategies that can be developed and utilized as translational biomarkers.

4) To establish a clinical trials and correlative infrastructure for the evaluation of survivorship and cognitive effects of ADT and Androgen receptor targeting therapies.

5) To develop novel therapeutic strategies for men with aggressive variant and/or small cell neuroendocrine prostate cancer.

6) To develop novel diagnostic and theranostic strategies utilized for the detection and treatment of men with recurrent or metastatic prostate cancer.

7) To streamline regulatory processes at UCSF for consortium trials, whether initiated by UCSF or other consortium members.

What was accomplished under these goals?

1) Adhere to performance metrics defined by Coordinating Center

As shown in the Appendix of this Final Progress Report, UCSF has accrued a total of 163 patients during the entire grant award period covering 09/30/2018 – 09/30/2022. Our average annual rate of accrual was 40.8 patients/year, exceeding the accrual metrics set forth in the DOD PCCTC grant. Of the patients accrued thus far, 12.3% were from disproportionately underrepresented patient populations.

During the cumulative grant award period covering 09/30/18 – 09/30/2022, UCSF serves or has served as the Lead Investigational Site for ten multi-center trials within the PCCTC, as outlined in the Appendix.

Within the reporting period, we have achieved several milestones for additional PCCTC trials:

1) ARN-509-002 (Lead site: UCSF; participating sites: U of Chicago, U of Washington, Mayo Scottsdale, Oregon Health & Science University). The manuscript has been published (see Appendix).
2) ZEN-002 study of the BET bromodomain inhibitor ZEN-3694 in combination with enzalutamide has completed study follow up and the database has been locked. The manuscript was published in Clinical Cancer Research (see list of of publications).
3) Phase 1b/2 study of ribociclib in combination with docetaxel. Database lock has occurred, and the manuscript was published in Clinical Cancer Research.
4) The Phase 1 FOR46 study accrual was completed, and the primary study results were presented as an oral abstract at the 2022 ASCO Annual Meeting. The manuscript for this study is currently under development.

2) Full participation in the consortium as a member of the Clinical Consortium Committee/ Scientific Oversight Committee

UCSF has participated in every scheduled DOD PCCTC PI monthly teleconference held during the reporting period. At the SOC meeting in February 2021, Rahul Aggarwal (PI) and UCSF Oncology Fellow Dr. Ivan de Kouchkovsky presented the final study results of the phase 1b/2 study of ribociclib in combination with docetaxel, and presented again as a follow up at the SOC meeting June 2022.

3) Leverage the integration of PCCTC clinical trials into tumor and DNA acquisition strategies that can be developed and utilized as translational biomarkers.

UCSF has integrated metastatic and liquid tumor biopsies into multiple PCCTC clinical trials, including:

1) A Phase 1b/2 Study of ZEN-3694 in Combination with Enzalutamide in Patients with Metastatic Castration Resistant Prostate Cancer (PI: Rahul Aggarwal)

2) A Phase 1, First-in-Human Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer (PI: Rahul Aggarwal)

3) A Phase 1/2 Study of Ribociclib in Combination with Docetaxel in Patients with Metastatic Castration Resistant Prostate Cancer (PI: Rahul Aggarwal)

4) 4) A Randomized, Phase II Study of Apalutamide +/- Stereotactic Body Radiotherapy (SBRT) in Castration-Resistant Prostate Cancer Patients with Oligometastatic Disease on PSMA-PET Imaging (PI: Rahul Aggarwal).

For all four of the PCCTC trials above, biopsied obtained at UCSF and other participating institutions are shipped to the Feng laboratory at UCSF for tissue processing, including laser capture microdissection of tumor tissue and RNA-seq profiling of fresh frozen biopsies. A separate biopsy core undergoes formalin fixation, and is embedded in paraffin. The FFPE blocks are analyzed using the Strata platform for targeted next-gen sequencing of tumor DNA, to evaluate for potentially targetable alterations (e.g. *BRCA2*). Tissue processing and sequencing is carried out using central, standardized methodology to ensure consistency of data across study cohorts.

Based on the acquisition of metastatic biopsies, Felix Feng and colleagues have recently published a comprehensive methylation profile of metastatic castration resistant prostate cancer biopsies in Nature Genetics (see Publications list). They have identified a newly described hypermethylated subset of mCRPC that is associated with favorable prognostic profile and may be targetable with epigenetic therapies. Biomarker development is underway to detect hypermethylated mCRPC for patient selection for targeted therapeutic trials. A manuscript describing the clinical outcomes of the hypermethylated subset of mCRPC has been submitted (under review, Clinical Cancer Research).

UCSF Hematology/Oncology faculty member Dr. Jonathan Chou has analyzed metastatic tumor tissue and cfDNA for presence of inactivating biallelic loss of CDK12, and has conducted pre-clinical research analyzing the functional impact of this genomic finding. These data were published as part of a whole genome sequencing landscape article in Cell (Quigley et al – see publication list below), as well as clinical outcomes in patients with tumors harboring CDK12 mutations (see publication list). These data form the scientific underpinning for a planned DOD PCCTC trial of ipilimumab + nivolumab in mCRPC patients harboring CDK12 mutations (IMPACT study, lead site: U of Michigan).

In conjunction with metastatic tumor biopsies, peripheral blood for analysis of circulating cell free DNA is collected for all patients enrolled on every therapeutic trial at UCSF, including the four PCCTC trials currently open at our site. We have activated a blood collection protocol (PI: Rahul Aggarwal and Felix Feng) to analyze presence of reversion mutations among patients receiving PARP inhibitor or platinum-based chemotherapy.

4) To establish a clinical trials and correlative infrastructure for the evaluation of survivorship and cognitive effects of ADT and Androgen receptor targeting therapies.

We have completed enrollment on our “STAND” randomized pilot study (PI: Rahul Aggarwal) investigating multi-disciplinary supportive care among men with prostate cancer within 6 months of initiating androgen deprivation therapy. The pilot feasibility data were presented at ASCO GU Symposium in February 2019 (Pollock et al). The overall study results indicate a high degree of feasibility with > 90% patient visit completion rate. Preliminary data suggests a trend towards improved quality of life and lessened metabolic toxicity (e.g. insulin resistance, increased body fat) compared with usual care treatment arm. The manuscript summarizing these results has been submitted for publication (under review, Urologic Oncology).

We have collaborated with Drs. Alicia Morgans (Northwestern University) and Charles Ryan (U of Minnesota) in the development of a randomized phase 2 study to evaluate the cognitive impact of AR targeting therapy in men with castration-resistant prostate cancer (“ARACOG”). The study is run through the Alliance Foundation, but relies on correlative science developed at UCSF including functional MRI brain imaging as a potential biomarker of early cognitive changes observed on androgen receptor targeting therapy. UCSF GU Oncology junior faculty member Dr. Hala Borno has integrated analysis of financial toxicity experienced by patients as a correlative biomarker in the ARACOG study.

We have completed enrollment to the CHAMP study (PI: Stacey Kenfield, UCSF), a randomized phase 2 study of supervised exercise training among men with minimally symptomatic metastatic castration resistant prostate cancer. The results demonstrate the feasibility of accruing with remote lifestyle interventions via web-based interface, and support the ongoing phase 3 study (GAP4, sponsored by Movember Foundation).

With the successful completion of STAND pilot study, and nearing completion of STAND, UCSF investigators (Aggarwal, Kenfield, June Chan, Hala Borno) have recently opened a follow on study to STAND ("STAND-T") leveraging community collaboration for a follow-on multi-institutional study of resistance exercise training, involving community oncology sites in the Greater Bay Area. The planned multi-institutional study will utilize web-based exercise instruction and activity monitoring to facilitate patient accrual and access to the study for men initiating treatment with androgen deprivation.

5) To develop novel therapeutic strategies for men with aggressive variant and/or small cell neuroendocrine prostate cancer.

Leveraging our SU2C/PCF/AACR West Coast Dream Team biopsy acquisition study, Drs. Aggarwal and Small published a prospective study analyzing the clinical and genomic features of treatment-emergent small cell neuroendocrine prostate cancer (Aggarwal et al. J Clin Oncol 2018 – see publication list). The results indicate an overall incidence of t-SCNC of 17% among all patients with mCRPC and a lesion amenable to percutanoues metastatic biopsy. This stands in stark contrast to the less than 1% incidence of *de novo* small cell prostate cancer detected at the time of diagnosis.

Leveraging these findings, Drs. Aggarwal and Small have helped develop a number of clinical trials to investigate novel therapies and treatment strategies for t-SCNC. These include:

- Led the basket study Phase 1b study of rovalpituzumab tesirine in patients with DLL3-expressing solid tumor malignancies. Study has been completed and manuscript has been submitted for publication.
- Analysis of the subset of patients with clinical and/or genomic features of t-SCNC treated on the PCCTC trial of oral BET inhibitor ZEN-3696 in combination with enzalutamide. This analysis has led to the successful grant application for a soon-to-open investigator-initiated trial of ZEN-3694 + enzautamide + pembrolizumab in patients with neuroendocrine prostate cancer. This trial has recently activated at UCSF, and University of Michigan will also be participating on this study.
- Development of anti-CD46 targeting drug FOR46 as a novel therapeutic strategy in t-SCNC. The therapeutic target and ADC (FOR46) were discovered in the Liu laboratory at UCSF, and the pre-clinical and translational results were published in JCI Insight (see publication list). The recently completed PCCTC phase 1 first-in-human study of FOR46 includes a Dose Expansion cohort for patients with histologic evidence of t-SCNC. Participating PCCTC institutions for this study include: Northwestern University, Oregon Health & Science University, University of California Los Angeles, and Karmanos Cancer Institute
- Analysis of t-SCNC tumors by whole genome sequencing, revealing distinct patterns of intra- and inter-tumoral heterogeneity with respect to t-SCNC differentiation. These results were published in March 2019 (Aggarwal et al. Molecular Cancer Research – see publication list)
- Ongoing collaboration with industry partner to develop a novel DLL3-targeting immunotherapy including investigation of DLL3 expression and treatment effect with patient-derived xenograft models of NEPC. The pre-clinical work is being performed by UCSF Hem/Onc fellow Dr. Jonathan Chou who is mentored by Dr. Felix Feng and Eric Small. This pre-clinical collaboration has fostesred UCSF leadership in the development of an upcoming Phase 1b/2 study of AMG 757, a CD3xDLL3 bi-specific Ab, in patients with *de novo* or treatment-emergent small cell neuroendocrine prostate cancer. The AMG757 study has been submitted as LOI to the DOD PCCTC with UCSF as the lead investigational site, with accrual ongoing.
- UCSF serves as the lead site for an ongoing phase 1b/2 study of pembrolizumab in combination with talabostat (Bioexcel Therapeutics, Inc.) focused on men with treatment-emergent or *de novo* small cell neuroendocrine prostate cancer. The study is currently accruing in the phase 2 portion of the study.

6) To develop novel diagnostic and theranostic strategies utilized for the detection and treatment of men with recurrent or metastatic prostate cancer.

Dr. Thomas Hope at UCSF has led a registrational study in collaboration with investigators at UCLA, investigating the use of 68Ga-PSMA PET as a diagnostic imaging tool for patients with biochemically recurrent prostate cancer. The study results were published in JAMA Oncology, indicating overall positive predictive value of PET lesion detection of > 90% (see publication citation below). Drs. Hope and Small

have undertaken a retrospective analysis of lesion detection rates among men with CRPC and no evidence of metastases by conventional imaging. The results indicate that over 90% of patients have PET-avid lesions. Dr. Hope has collaborated with investigators at UCLA to demonstrate improved sensitivity for lesion detection by PSMA vs. fluciclovine PET (see Publication List). PSMA PET imaging was recently FDA approved for use at UCSF and UCLA for the detection of disease in the newly diagnosed and biochemically recurrent settings.

Building upon these results, Drs. Aggarwal, Hope, Feng, and Small have designed a randomized phase 2 study of apalutamide with or without stereotactic body radiation therapy to oligometastatic sites of disease on PSMA PET among patients with CRPC. The study has been accepted for distribution within the PCCTC, and participating PCCTC sites include U of Wisconsin (PI: Glenn Liu). Study enrollment at UCSF is ongoing and we expect activation at U of Wisconsin within next 3 months.

Dr. Aggarwal and Hope have extended diagnostic PSMA PET to develop theranostic treatment strategies for patients with metastatic castration resistant prostate cancer. Dr. Aggarwal and Hope lead an active investigator-initiated trial evaluating a priming dose of ^{177}Lu-PSMA-617 followed by checkpoint blockade with pembrolizumab in patients with chemotherapy-naïve metastatic castration resistant prostate cancer. The Phase 1 dose finding portion of the study has recently been completed and results will be presented at the ASCO 2021 meeting. The phase 2 portion of the study will include additional PCCTC sites (list TBD).

Dr. Aggarwal and Dr. Michael Evans, a radiochemist within the Nuclear Medicine imaging group, have developed transferrin-based PET using ^{68}Ga-citrate as a potential biomarker of aggressive variant prostate cancer with evidence of neuroendocrine differentiation. We have integrated pre/post Ga-citrate PET imaging in the PCCTC trial of ribociclib in combination with docetaxel, as well as the Phase 1 study of ZEN-3694 in combination with enzalutamide. This work has led to a DOD Idea Development and Idea Expansion Award.

Dr. Aggarwal, in conjunction with colleagues in the Department of Radiology, have translated a first-in-human novel PSMA-targeting radioligand, CTT1403, for the treatment of metastatic castration resistant prostate cancer. The study is currently in dose escalation and plans to expand to additional sites within PCCTC during Dose Expansion, including the University of Washington and UCLA.

Dr. Aggarwal and Dr. Michael Evans have developed a novel PET radiotracer that avidly and specifically binds to the glucocorticoid receptor (GR), and have developed an investigator-initiated trial supported by Oric Pharmaceuticals to investigate enzalutamide + ORIC-101 (a novel potent GR antagonist) in men with metastatic castration resistant prostate cancer and resistance to at least one prior androgen signaling inhibitor (see Publication list). This study will be distributed through the Prostate Cancer Clinical Trials Consortium.

7) To streamline regulatory processes at UCSF for consortium trials, whether initiated by UCSF or other consortium members.

UCSF has implemented a pilot program to expedite the activation of consortium and industry-sponsored trials, by assigning a dedicated budget analyst linked to an individual PI. The target timeline is 120 days from the date of approval by the Scientific Review Committee at UCSF. As of the most recent metrics of trial activation, the average time to activation has averaged 156 days, an improvement compared to prior but still indicating further need for improving efficiency of the trial activation process. In addition, the UCSF IRB has expanded the applicability of use of central IRB for the oversight of phase 2 and 3 studies, which will help expedite study activation as well.

Dr. Hala Borno, a faculty member within the UCSF Prostate Cancer program, has recently developed a Clincal Trial Matching Tool (www.ucsftrials.com) that has been widely utilized to facilitate clinical trial referrals from community oncologists and affiliate sites. Pilot data indicate this web-based tool has significantly increased provider satisfaction and knowledge of currently available prostate cancer trials at UCSF, and has led to increased referrals for clinical trial participation including from rural populations in the Central Valley of California.

Describe the Regulatory Protocol and Activity Status (if applicable).

Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state "Nothing to Report."

(a) ***Human Use Regulatory Protocols***

Nothing to report

(b) Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

TOTAL ACTIVITIES: *No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW)."*

(c) Animal Use Regulatory Protocols

TOTAL PROTOCOL(S): *No animal use research will be performed to complete the Statement of Work."*

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

We plan to initiate and/or continue accrual to the following DOD PCCTC multi-center trials in which UCSF serves as the lead academic site:

1) A Phase 1, First-in-Human Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer (PI: Rahul Aggarwal). The study has recently completed accrual. We plan to achieve database lock and publication of study results.

2) A randomized phase 2 study of apalutamide with or without stereotactic body radiation to PSMA PET-avid sites of disease in oligometastatic CRPC. We plan to complete study accrual with UCSF and participating sites (U of Wisconsin).

3) A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), adiminstered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer. We plan to initiate phase 2b of study accrual.

4) Phase 2 study of AMG757, in patients with neuroendocrine prostate cancer. We plan to complete study accrual.

5) Pembrolizumab in combination with ZEN-3694 plus enzalutamide in patients with mCRPC (Investigator-initiated trial; UCSF lead site; U of Michigan participating site). We plan to complete study accrual to the transdifferentiated cohort of this study.

4. Impact

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

The phase 2 trial (ARN-509-002) with LHRH agonist + apalutamide demonstrated a trend towards improved PSA progression-free survival without detriment with respect to quality of life or delayed time to testosterone recovery in men with biochemically recurrent prostate cancer has led to the development of an ongoing phase 3 trial testing the combination as compared with standard of care ADT (Alliance Foundation trial-19; national PI: Rahul Aggarwal). The results from the Phase 3 study were presented at ESMO 2022 and demonstrate significant prolongation of PSA progression-free survival in patients treated with intensified androgen deprivation with addition of apalutamide with or without abiraterone.

The recently completed Phase 1b/2 study of ZEN-3694 plus enzalutamide has demonstrated encouraging activity in AR-indifferent mCRPC and has fostered the development of a follow-in phase 2 study of ZEN-3694 plus pembrolizumab plus enzalutamide in patients with de-differentiated mCRPC. Accrual to the randomized phase 2 study is ongoing.

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. Changes/Problems.

Changes in approach and reasons for change

Nothing to Report

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

COVID-19 previously impacted patient accrual though recovery is now ongoing with current accrual across the Cancer Center up to ~ 90% of pre-COVID levels.

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Significant changes in use or care of vertebrate animals.

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. Products

Publications include the following:

1. Aggarwal R, Alumkal JJ, Szmulewitz R, et al. A randomized phase II study of apalutamide, androgen deprivation therapy, or apalutamide plus androgen deprivation therapy in patients with biochemically relapsed prostate cancer. J Clin Oncol 38, 2020 (suppl 6; abstr 320)
2. Reimers MA, Yip SM, Zhang L, et al. Clinical outcomes in Cyclin-dependent kinase 12 mutant advanced prostate cancer. European Urology 2020;77:333-41.

3. Aggarwal R, Huang J, Alumkal J, Zhang L, Feng F, Thomas G, Weinstein AS, Friedl V, Zhang C, Witte O, Lloyd P, Gleave M, Evans CP, Youngren J, Beer T, Rettig M, Wong C, True L, Foye A, Playdle D, Ryan CJ, Lara P, Chi K, Uzunangelov V, Sokolov A, Beltran H, Demichelis F, Rubin MA, Stuart J, and Small EJ. Clinical and Genomic Characterization of Treatment-Emergent Small Cell Neuroendocrine Prostate Cancer: a Multi-Institutional Prospective Study. J Clin Oncol 2018; 36(24):2492-2503. PMID: 29985747

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8. Aggarwal R, Schweizer M, Pantuck A, Nanus D, Pantuck AJ, Heath EI, Campeau E, Attwell S, Norek K, Snyder M, Bauman L, Lakhotia S, Feng FY, Small EJ, Abida W, and Alumkal J. A phase 1b/2a study of the BET bromodomain inhibitor ZEN-3694 in combination with enzalutamide in patients with metastatic castration-resistant prostate cancer. Clinical Cancer Research 2020;26:5338–47.

9. Fendler WP, Calais J, Eiber M, Flavell RR, Mishoe A, Feng FY, Nguyen HG, Reiter RE, Rettig MB, Okamoto S, Emmett L, Zacho HD, Ilhan H, Wetter A, Rischpler C, Schoder H, Burger IA, Garmann J, Smith R, Small EJ, Slavik R, Carroll PR, Herrmann K, Czernin J, and Hope TA. JAMA Oncology 2019; 5(6):856–63.

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16. Borno HT, Zhang L, Zhang S, Kaplan C, Palmer NR, Bell A, Bakke B, Lin A, Aggarwal R, Small EJ. A mobile clinical trial matching technology in medical oncology clinic: a pilot feasibility study. JCO Clinical Cancer Informatics 2022 [in press; accepted for publication 4 MAR 2022

7. Participants and Other Collaborating Organizations

What individuals have worked on the project?

Name:	Rahul Aggarwal, MD, no change
Name:	Eric Small, MD, no change
Name:	Kaleas Johnson, no change
Name:	Patricia Li, no change

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?
Academic Institutions:

Organization Name: Oregon Health & Science University
Location of Organization: Portland, OR
Partner's contribution to the project:
OHSU is a participating site on the following trials: FOR46, ARN-509-002, ZEN-3694 + enzalutamide

Organization Name: University of Washington
Location of Organization: Seattle, Washington
Partner's contribution to the project:
University of Washington is a participating site on the following projects: ARN-509-002

Organization Name: The University of Chicago
Location of Organization: Chicago, Illinois
Partner's contribution to the project:
The University of Chicago is a participating site on the following projects: Ribociclib + docetaxel, ARN-509-002

Organization Name: Northwestern
Location of Organization: Evanston, IL
Partner's contribution to the project:
Northwestern is a participating site for the following projects: Ribociclib + docetaxel, FOR46

Organization Name: University of Michigan
Location of Organization: Ann Arbor, MI

Partner's contribution to the project:
University of Michigan is a participating site for the following projects: Ribociclib + docetaxel

Organization Name: University of Wisconsin
Location of Organization: Madison, WI
Partner's contribution to the project:
The University of Wisconsin is a participating site for the upcoming randomized phase 2 study of apalutamide +/- SBRT in oligometastatic CRPC.

Organization Name: Memorial Sloan Kettering Cancer Center
Location of Organization: New York City, NY
Partner's contribution to the project (c15-165)
Memorial Sloan Kettering Cancer Center is a lead site on: CC-115 + enzalutamide

Organization Name: University of California Los Angeles
Location of Organization: Los Angeles
Partner's contribution to the project (c15-165)
The University of California Los Angeles is a participating site on the following projects: FOR46, apalutamide +/- SBRT, ZEN-3694 + enzalutamide

Industry & Other Contributions:

Organization Name: Janssen
Location of Organization: Headquarters – Titusville, New Jersey
Partner's contribution to the project:
Janssen is provides financial support, and manufactures and supplies the study drug for apalutamide +/- SBRT, and ARN-509-002

Organization Name: Novartis
Location of Organization: Headquarters – Basel, Switzerland
Partner's contribution to the project:
Novartis provides financial support and supply of the study drug for project: Ribociclib + docetaxel

Organization Name: Zenith Epigenetics
Location of Organization: US Office – San Francisco, CA
Partner's contribution to the project:
Zenith Epigenetics provides financial support, and the study drug for project ZEN-3694 + enzalutamide.

Organization Name: Celgene Corporation
Location of Organization: San Francisco, CA
Partner's contribution to the project:
Celgene Corporation provides financial support, and the study drug for project: CC-115 + enzalutamide

Organization Name: Fortis Therapeutics, Inc.
Location of Organization: La Jolla, CA
Partner's contribution to the project:
Fortis Therapeutics provides financial support, and the study drug for project FOR46.

8. Special Reporting Requirements

Nothing to Report.

9. APPENDICES:

SUPPORTING DATA:
University of California, San Francisco
Table A. Trials Introduced by UCSF (as of 03/31/2021)
Table B. Patient Accrual by UCSF during current grant award period (09/30/2018 – 03/31/2022)
Table C. Patient Accrual by UCSF during the progress report period (10/1/2021 – 03/31/2022)

Table A. Trials Introduced by UCSF (As of 10/1/2021)

Target Accrual	Accrual - UCSF	IRB Approval Date	Open to Accrual Date	Closed to Accrual Date	Participating PCCTC Sites
LOI# c12-102: The Role of Highly Selective Androgen Receptor (AR) Targeted Therapy in Men with Biochemically Relapsed Hormone Sensitive Prostate Cancer <PI:R. Aggarwal>					
90	40	4/18/2012	2/13/2013	08/01/2016	**OHSU, Washington, Chicago**
LOI# c15-149: A Phase 1b/2 Study of the Oral CDK4/6 Inhibitor LEE011 (Ribociclib) in Combination with Docetaxel plus Prednisone in Metastatic Castration Resistant Prostate Cancer <PI:R. Aggarwal>					
47	41	04/28/2015	9/25/2015	3/2019	**Northwestern, Michigan, U of Chicago, Brown University, University of Minnesota**
LOI# c15-157: A Phase 1 Study of ES414 in Patients with Metastatic Castration-Resistant Prostate Cancer <PI:L. Fong>					
125	7	02/23/2015	4/13/2015	6/2019	**Washington, OHSU, Michigan, Wisconsin, Duke, Chicago, Weill Cornell**
LOI# c15-165: A Phase 1 Safety and Tolerability Study of ZEN003694 in Patients with Metastatic Castration-resistant Prostate Cancer <PI:R. Aggarwal>					
44	9	3/6/2016	5/6/2016	10/1/2017	**OHSU, MSKCC, UCLA, WSU**
LOI# c15-166: A Phase 1 Safety and Tolerability Study of ZEN003694 in Combination with Enzalutamide in Patients with Metastatic Castration-Resistant Prostate Cancer <PI:R. Aggarwal>					
58	15	5/5/2016	11/15/2016	11/2019	**OHSU, MSKCC, UCLA, WSU**
c18-221: A Phase 1b Dose Escalation/Expansion Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer <PI: R. Aggarwal>					
42	24	12/13/2018	2/4/2019	Accrual ongoing	**OHSU, UCLA, Northwestern, Karmanos**

c19-242: A randomized phase 2 study of apalutamide with or without stereotactic body radiation to PSMA PET-avid sites of disease in oligometastatic CRPC <PI: R. Aggarwal>					
60	13	6/15/2019	12/15/2019	Accrual ongoing	**Wisconsin**
c20-263: A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), adiminstered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer <PI: R. Aggarwal>					
68	17	5/1/2019	10/3/2019	Accrual ongoing	**Weill-Cornell, Ohio State University, Moffitt Cancer Center**
c21-273: 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 <PI: R. Aggarwal>					
10	3	8/5/2021	11/8/2021	Accrual ongoing	
c21-285: A Phase 2 Study of BET Bromodomain Inhibitor ZEN-3694 in Combination with Enzalutamide Plus Pembrolizumab in Metastatic Castration Resistant Prostate Cancer <PI: R. Aggarwal>					
54	24	6/10/2020	12/7/2020	Accrual ongoing	**Michigan**
c22-312: A Modular Phase 2a Multicentre Open-Label Study to Investigate DNA-damage Response Agents (or Combinations) in Patients with Advanced Cancer Whose Tumours Contain Molecular Alterations (PLANETTE) <PI: R. Aggarwal & W. Abida>					
52	9	3/7/2021	10/7/2021	Accrual ongoing	

Table B. Accrual in Grant Award Period (09/30/2018 – 09/30/2022)

PCCTC #	Lead Institution	Study Title	Patient Accrual 9/30/2018 - 9/30/2019	Patient Accrual 10/1/2019 – 3/31/2020	Patient Accrual 4/1/2020 – 9/30/2020	Patient Accrual 9/30/2020 – 3/31/2021	Patient Accrual 4/1/2021 – 9/30/2021	Patient Accrual 10/1/2021 – 3/31/2022	Patient Accrual 4/1/2022 – 9/30/2022	Patient Accrual Total Grant Award Period 9/30/18 – 9/30/22
c15-149	UCSF	Tax/LEE	12	0	0	0	0	0	0	12
c15-166	UCSF	Zen/Enza	9	0	0	0	0	0	0	9
c18-221	UCSF	FOR46	7	2	1	4	6	6	1	27
c19-242	UCSF	PILLAR	0	0	2	2	3	6	3	16
c19-244	OHSU	ARV-110	0	0	0	0	2	1	0	3
c15-160	MSKCC	CC-115 + Enzalutamide	1	0	0	0	0	0	0	1
c18-219	JHU	COMBAT	0	0	4	0	0	0	0	4
c18-225	UMich	IMPACT	0	0	5	1	1	0	0	7
c19-241	UCSF	Poseida	0	0	0	0	0	3	3	6
c20-259	UWash	Janssen CD3xPSMA BiTE	0	0	1	3	2	0	0	6
c20-257	Columbia	HPN424	0	3	4	1	2	0	0	10
c20-263	UCSF	BXCL701	0	4	0	7	3	3	3	20
c21-282	TJU	AMG 509	0	0	0	0	0	0	1	1
c20-268	JHU	ARCUS	0	0	0	0	0	0	0	0
c21-273	UCSF	AMG 757	0	0	0	0	0	1	3	4
c21-278	OHSU	GAP4	0	0	0	0	0	0	0	0
c21-284	MSKCC	AMG 160	0	0	0	0	0	1	0	1
c21-285	UCSF	ZEN-3694	0	0	0	2	6	16	2	26
c22-298	UCSF/U of Michigan	Enzalutamide +/- ZEN-3694	0	0	0	0	0	0	1	1
c22-312	UCSF	PLANETTE	0	0	0	0	0	6	3	9
Total Accrual			**29**	**9**	**17**	**20**	**25**	**43**	**20**	**163**

Table D. Accrual in Semi-Annual Period (4/1/2022 – 9/30/2022)

PCCTC #	Lead Institution	Study Title	Patient Consents Between 4/1/2022 – 9/30/2022	Patient Enrollment Accrual Between 4/1/2022 – 9/30/2022
c18-221	UCSF	FOR46	0	1
c19-242	UCSF	PILLAR	4	3
c19-244	UCSF	ARV-110	0	0
c18-225	UMich	IMPACT	0	0
c19-241	UCSF	Poseida	1	3
c20-259	UWash	CD3xPSMA BiTE/ JNJ-63898081	0	0
c20-257	Columbia	HPN424	0	0
c20-263	UCSF	BXCL701	4	3
c20-264	TJU	AMG 509	2	1
c20-268	JHU	ARCUS	0	0
c21-273	UCSF	AMG 757	2	3
c21-278	OHSU	GAP4	4	0
c21-284	MSKCC	AMG 160	0	0
c21-285	UCSF	ZEN-3694	6	2
c22-298	UCSF/U of Michigan	Enzalutamide +/- ZEN-3694	1	1
c22-312	UCSF	PLANETTE	6	3
Total Number			**30**	**20**