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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 12 month reporting period from 9/30/2020 through 9/30/2021, 46 patients were enrolled across eight PCCTC clinical trials, including four trials led by UCSF. During the reporting period, one UCSF-led LOI has been submitted for phase 1b/2 study of AMG 757, a bi-specific T cell engager targeting DLL3 and CD3 in neuroendocrine prostate cancer.					
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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 Annual Progress Report, UCSF has accrued a total of 101 patients during the entire grant award period covering 09/30/2018 – 09/30/2021. In this annual progress reporting period from 09/30/2020 – 09/30/2021, UCSF has enrolled 46 patients to 8 PCCTC trials, including four trials led by UCSF. Of the 101 total patients accrued during the entire grant award period to date, 31 patients have been accrued onto clinical trials led by other consortium sites. Over the course of the 36 month grant award period to date, our average rate of accrual is 33.7 patients/year, exceeding the minimum accrual metrics set forth in the DOD PCCTC grant. Of the 101 patients accrued thus far, 13 patients (12.9%) are from disproportionately underrepresented patient populations.

During the cumulative grant award period covering 09/30/18 – 09/30/2021, UCSF serves or has served as the Lead Investigational Site for six multi-center trials within the PCCTC, as follows:

1) A Phase 1b/2 Study of ZEN-3694 in Combination with Enzalutamide in Patients with Metastatic Castration Resistant Prostate Cancer (National PI: Rahul Aggarwal). Participating DOD PCCTC sites: UCLA, Memorial Sloan Kettering, Oregon Health & Science University, Karmanos Cancer Institute.

2) A Phase 1, First-in-Human Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer (National PI: Rahul Aggarwal). Participating DOD PCCTC sites: UCLA, Oregon Health & Science University, Northwestern University, Karmanos Cancer Institute.

3) A Phase 1/2 Study of Ribociclib in Combination with Docetaxel in Patients with Metastatic Castration Resistant Prostate Cancer (National PI: Rahul Aggarwal). Participating DOD PCCTC sites: University of Chicago, University of Minnesota.

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 (National PI: Rahul Aggarwal). Participating DOD PCCTC sites: University of Wisconsin (site PI: Glenn Liu).

5) A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), administered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer (National PI: Rahul Aggarwal).

6) A Phase 2 Study of BET Bromodomain Inhibitor ZEN-3694 in Combination with Enzalutamide Plus Pembrolizumab in Metastatic Castration Resistant Prostate Cancer (National PI: Rahul Aggarwal)

In the annual reporting period, we have submitted two LOIs: 1) Phase 2 study of AMG 757, a bi-specific T cell engager targeting DLL3 in neuroendocrine prostate cancer, and 2) Pembrolizumab, ZEN-3694, and enzalutamide in patients with de-differentiated metastatic castration resistant prostate cancer, building upon the initial data in the Phase 1b/2 study of ZEN-3694 plus pembrolizumab. This study will be opened thru PCCTC with University of Michigan serving as a participating site.

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 submitted for publication (under review; Urologic Oncology).

2) ZEN-002 study of the BET bromodomain inhibitor ZEN-3694 in combination with enzalutamide was published in Clinical Cancer Research (see list of publications).

3) Phase 1b/2 study of ribociclib in combination with docetaxel. Database lock has occurred, and the manuscript is planned for submission Q4 2021.

4) Interim results from the ongoing Phase 1, first-in-human study of FOR46 were presented at the ESMO 2021 Annual Meeting.

5) Interim results from the ongoing Phase 1/2 study of BXCL701 in combination with pembrolizumab were presented at the ESMO 2021 Annual Meeting.

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 May 2021 PI teleconference, Rahul Aggarwal (PI) and UCSF Radiologist Dr. Robert Flavell presented interim results of the phase 1 study of FOR46 in patients with metastatic castration resistant prostate cancer, including development of a novel CD46-targeting PET tracer.

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).
- 5) A Phase 2 Study of BET Bromodomain Inhibitor ZEN-3694 in Combination with Enzalutamide Plus Pembrolizumab in Metastatic Castration Resistant Prostate Cancer (PI: Rahul Aggarwal)

For the five PCCTC trials above, biopsies 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. Within the grant award period, of the 101 patients enrolled on PCCTC trials at UCSF, 55% have undergone metastatic tumor biopsies prior to enrollment on PCCTC trial. Data analyses from the tissue biopsies is ongoing including potential biomarkers of response to BET inhibition, CDK 4/6 inhibitors, and other novel targeted agents (e.g. FOR46 targeting CD46 expressed on surface of prostate cancer metastases).

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, *Journal Precision Oncology*). Aggarwal et al. recently published a study in mCRPC describing outcomes by luminal versus basal subtyping of mCRPC biopsies using the PAM50 classifier (see Publications list).

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. A manuscript describing 5-hydroxymethyl cytosine (5hmc) sequencing of circulating tumor DNA is under preparation for submission.

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 was recently published in Urologic Oncology (see Publications list).

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 will be run through the Alliance Foundation, but will rely in part on correlative science developed at UCSF including fMRI 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 were recently published in Cancer Medicine (see Publications list).

With the successful completion of STAND pilot study, and nearing completion of STAND, UCSF investigators (Aggarwal, Kenfield, June Chan, Hala Borno) are planning on 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 percutaneous 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 the results were recently published (see Publications list).
- 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 an ongoing investigator-initiated trial of ZEN-3694 + enzautamide + pembrolizumab in patients with neuroendocrine prostate cancer. 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 ongoing 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 fostered 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 recently been submitted as LOI to the DOD PCCTC with UCSF as the lead investigational site. A manuscript describing the pre-clinical data with AMG 757 in NEPC models is under preparation.
- 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 list). 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: Christos Kyriakopoulos). 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 ¹⁷⁷Lu-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 ⁶⁸Ga-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.

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 138 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 junior faculty member within the UCSF Prostate Cancer program, has recently developed a clinical trial algorithm (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 will lead to increased referrals for clinical trial accrual.

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 is currently accruing in Dose Expansion.
- 2) A randomized phase 2 study of apalutamide with or without stereotactic body radiation to PSMA PET-avid sites of disease in oligometastatic CRPC.
- 3) A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), administered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer
- 4) Phase 2 study of AMG757, in patients with neuroendocrine prostate cancer
- 5) Pembrolizumab in combination with ZEN-3694 plus enzalutamide in patients with mCRPC (Investigator-initiated trial; UCSF lead site; U of Michigan participating site).

UCSF is continuing to accrue to several additional PCCTC clinical trials led by other institutions within the PCCTC, including the following:

- 1) IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations; (UCSF PI: Eric Small and Jonathan Chou)
- 2) Phase 1 study of HPN24 (UCSF PI: Lawrence Fong)

UCSF is planning on initiating accrual to the following investigator-initiated trials led by other PCCTC sites during the next 6 months:

- 1) BrUOG 360: A Phase 1b/2 Study of Copanlisib Combined with Rucaparib in Patients with Metastatic Castration-Resistant Prostate Cancer; Lead Investigational Site: Brown University; UCSF PI: Rahul Aggarwal
- 2) A Parallel Arm Phase 1b/2a Study of DKN-01 as Monotherapy or in Combination With Docetaxel for the Treatment of Advanced Prostate Cancer With Elevated DKK1. Lead Investigational Site: New York University; UCSF PI: Rahul Aggarwal

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 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, as well as an ongoing randomized phase 2 study of enzalutamide with or without ZEN-3694 in mCRPC.

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 ~ 70% 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.
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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:	Kaitlin Zablotsky GU Program Manager
Name:	Kelly Chao, Clinical Research Coordinator

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.

Academic Institutions (Continued)

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 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 09/30/2021)

Table B. Patient Accrual by UCSF during current grant award period (09/30/2018 – 09/30/2021)

Table C. Patient Accrual by UCSF during the progress report period (09/30/2020 – 9/30/2021)

Table A. Trials Introduced by UCSF (As of 09/30/2021)

Target Accrual	Accrual - UCSF	IRB Approval Date	Open to Accrual Date	Closed to Accrual Date	Participating PCCTC Sites
<i>c12-102: The Role of Highly Selective Androgen Receptor (AR) Targeted Therapy in Men with Biochemically Relapsed Hormone Sensitive Prostate Cancer <PI:R. Aggarwal></i>					
90	40	4/18/2012	2/13/2013	08/01/2016	OHSU, Washington, Chicago
<i>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></i>					
47	37	04/28/2015	9/25/2015	3/2019	Northwestern, Michigan, U of Chicago, Brown University, University of Minnesota
<i>c15-157: A Phase 1 Study of ES414 in Patients with Metastatic Castration-Resistant Prostate Cancer <PI:L. Fong></i>					
125	7	02/23/2015	4/13/2015	6/2019	Washington, OHSU, Michigan, Wisconsin, Duke, Chicago, Weill Cornell
<i>c15-165: A Phase 1 Safety and Tolerability Study of ZEN003694 in Patients with Metastatic Castration-resistant Prostate Cancer <PI:R. Aggarwal></i>					
44	8	3/6/2016	5/6/2016	10/1/2017	OHSU, MSKCC, UCLA, University of Washington
<i>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></i>					
58	15	5/5/2016	11/15/2016	11/2019	OHSU, MSKCC, UCLA, University of Washington
<i>c18-221: A Phase 1b Dose Escalation/Expansion Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer <PI: R. Aggarwal></i>					

42	17	12/13/2018	2/4/2019	Accrual ongoing	OHSU, UCLA, Northwestern, Karmanos
<i>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></i>					
60	7	6/15/2019	12/15/2019	Accrual ongoing	Wisconsin
<i>c20-263: A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), administered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer <PI: R. Aggarwal></i>					
68	12	5/1/2019	10/3/2019	Accrual ongoing	Weill-Cornell, Ohio State University, Moffitt Cancer Center
<i>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></i>					
48	8	6/10/2020	3/8/2021	Accrual ongoing	University of Michigan
<i>c21-285: 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></i>					
50	0	8/4/2021	Not yet open to accrual	Accrual activation pending	Washington University

Table B. Accrual in Grant Award Period (09/30/2018 – 09/30/2021)

PCCTC #	Lead Institution	Study Title	Patient Accrual 10/2018 – 3/2019	Patient Accrual 4/2019 – 9/2019	Patient Accrual 10/2019 – 3/2020	Patient Accrual 4/2020 – 9/2020	Patient Accrual 10/2020 – 3/2021	Patient Accrual 4/2021 – 9/2021	Patient Accrual Total Grant Award Period 10/2018 – 9/2021
c15-149	UCSF	Tax/LEE	7	5	0	0	0	0	12
c15-166	UCSF	Zen/Enza	8	1					9
c18-221	UCSF	FOR46	2	5	2	1	4	4	18
c18-242	UCSF	PILLAR				2	2	5	9
c19-244	OHSU	ARV-110					2	2	2
c15-160	MSKCC	CC-115 + ENZ	0	1					1
c18-219	JHU	COMBAT				4	0	0	4
c18-225	UMich	IMPACT				5	2	1	8
c20-259	U Wash	JNJ-63898081				1	3	2	6
c20-257	Columbia	HPN424			3	4	1	2	10
c20-263	UCSF	BXCL701			4	0	7	3	14
c21-285	UCSF	Pembro/Zen/ Enza					2	6	8
Total Accrual			17	12	9	17	21	25	101

Note: The grey shaded regions represent time intervals when each trial was not open to accrual at UCSF. Patient accrual for each PCCTC trial over each six month interval is shown.

Table D. Accrual in Progress Report Period (09/30/2020 – 09/30/2021)

PCCTC #	Lead Institution	Study Title	Patient Enrollment Accrual Between 9/30/2020 – 9/30/2021
c18-221	UCSF	<i>A Phase 1b Dose Escalation/Expansion Study of FOR46 in Patients with Metastatic Castration Resistant Prostate Cancer</i>	8
c19-242	UCSF	<i>A randomized phase 2 study of apalutamide with or without stereotactic body radiation to PSMA PET-avid sites of disease in oligometastatic CRPC</i>	7
c19-244	OHSU	<i>A phase 1, open-label, dose escalation clinical trial to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARV-110 in patients with metastatic castration-resistant prostate cancer who have progressed on least two prior systemic therapies.</i>	2
c18-225	University of Michigan	<i>IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations</i>	3
c20-259	University of Washington	<i>A Phase 1, First-in-Human, Dose Escalation Study of JNJ-63898081 in Subjects with Advanced Stage Solid Tumors</i>	5
c20-257	Columbia University	<i>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</i>	3
c20-263	UCSF	<i>A Phase 1b/2 Study of BXCL701, a small molecule inhibitor of dipeptidyl peptidases (DPP), administered in combination with anti-programmed cell death 1 (PD-1) monoclonal antibody pembrolizumab, in patients with small cell neuroendocrine prostate cancer</i>	10
c21-285	UCSF	<i>A Phase 2 Study of BET Bromodomain Inhibitor ZEN-3694 in Combination with Enzalutamide Plus Pembrolizumab in Metastatic Castration Resistant Prostate Cancer</i>	8
Total Accrual			46