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14. ABSTRACT

Purppose: 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 reporting period, 32 patients were accrued across four PCCTC clinical trials, including three trials led by UCSF. One additional LOI was presented at the Scientific Oversight Committee for a PSMA-directed SBRT trial in oligometastatic CRPC.

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 Annual Progress Report (see Pages 19–20), UCSF has accrued 32 patients onto 4 DOD PCCTC clinical trials during the reporting period of 09/30/2018 – 09/30/2019. Of the 32 patients accrued, 2 subjects have been accrued onto clinical trials led by other consortium sites. With the upcoming activation of several additional PCCTC trials from other institutions, we expect to accrue at least 20% of patients to trials from other consortium sites over the next annual reporting period.

Of the 32 patients accrued in Year 1, 6 patients (19%) are from disproportionately underrepresented patient populations, including 4 African-American patients and 2 Hispanic patients.

During the reporting period of 09/30/18 – 09/30/2019, UCSF serves as the Lead Investigational Site for three 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. We have successfully completed accrual to this investigator-initiated trial within the prior annual reporting period.

During the reporting period, we have proposed one accepted LOI within the PCCTC:

1) A Randomize, Phase 2 Study of Apalutamide +/- Stereotactic Body Radiotherapy (SBRT) in Castration-Resistant Prostate Cancer Patients with Oligometastatic Disease on PSMA PET Imaging. The proposed study leverages UCSF's institutional expertise with PSMA PET as a novel molecular imaging tool to enhance the sensitivity of metastatic lesion detection. The study will be opening at two additional sites within the PCCTC: University of Wisconsin (PI: Glenn Liu) and University of California Los Angeles (PI: Matt Rettig).

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

1) cc- ARN-509-002 (Lead site: UCSF; participating sites: U of Chicago, U of Washington, Mayo Scottsdale, Oregon Health & Science University). Patient follow up has been completed and database locked as of March 2019. Data analyses of the primary, secondary, and correlative endpoints has been completed and submission clinical trial data for presentation at the ASCO GU Symposium in 2020 has been completed.

2) ZEN-001 study of single agent ZEN-3694 has completed accrual and patient follow up. The data were presented at the AACR conference this year (Atlanta, GA – see list of publications).

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 on the third Thursday of every month during the reporting period. Dr. Eric Small (Co-Principal Investigator, UCSF) presented the FOR46 Phase 1 trial concept on the PI teleconference September 2018. Rahul Aggarwal (site PI) has attended the in-person Scientific Oversight Committee meetings held throughout the year. In this reporting period, Dr. Aggarwal attending the Oversight Committee meetings in October 2018 at the Prostate Cancer Foundation annual meeting, at the ASCO GU Symposium in February 2019 in San Francisco, CA, and the 2019 ASCO Annual Meeting in June in Chicago, IL. Upcoming meetings including the SOC meeting at the Prostate Cancer Foundation retreat on 10/23/2019. At this SOC meeting, Rahul Aggarwal (PI) will be presenting the new LOI of apalutamide +/- stereotactic body radiation as outlined above.

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 baseline metastatic 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)

For all three 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.

Within the reporting period, of the 32 patients enrolled on PCCTC trials at UCSF, 24 (75%) 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).

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.

UCSF Hematology/Oncology fellow 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), and 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). Jon Chou and colleagues have also recently had an accepted manuscript to European Urology describing the clinical outcomes of CDK12-mutated prostate cancer.

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 results of this study are being prepared for a manuscript submission planned in the first quarter of 2020.

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 continue to enroll patients at UCSF on CHAMP (PI: Stacey Kenfield, UCSF), a randomized phase 2 study of supervised exercise training among men with minimally symptomatic metastatic castration resistant prostate cancer. Study accrual is anticipated to be completed within

With the successful completion of STAND pilot study, and nearing completion of STAND, UCSF investigators (Aggarwal, Kenfield, June Chan) 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 activiy monitoring to facilitate patient accrual and access to the study.

Rahul Aggarwal and Stacey Kenfield, along with UCSF GU Oncology fellow Daniel Kwon, have participated in the newly formed SuRECaP (Survivorship Research in Prostate Cancer) Working Group. We have recently had a white paper describing survivorship challenges in prostate cancer accepted for publication in Urologic Oncology: Seminars and Original Investigations.

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 neuroendocrine prostate cancer cohort of the PCCTC study Phase 1b study of rovalpituzumab tesirine in patients with DLL3-expressing solid tumor malignancies. Overall UCSF accrued 5 patients to the NEPC cohort of this study. The study database was recently locked, and planned manuscript submission in first half of 2020.

- 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 new investigator-initiated trial fo ZEN-3694 + enzautamide + pembrolizumab in patients with neuroendocrine prostate cancer.
- 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.

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 recently 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.

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 will be proposed to be conducted within the PCCTC, and participating PCCTC sites include: UCLA (PI: Matt Rettig) and U of Wisconsin (PI: Glenn Liu).

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 will be conducted at UCSF alone, however additional PCCTC sites will be considered in Dose Expansion portion of the study. First patient was enrolled on this study in July 2019.

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.

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. 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.

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 continue accrual to the following DOD PCCTC trials:

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

A Phase 1b study of CC-115 in combination with enzalutamide in patients with metastatic castration resistant prostate cancer.

UCSF has submitted a new PCCTC LOI that has been accepted to move forward. This is an upcoming investigator-initiated randomized phase 2 study to propose for activation within the PCCTC, entitled “A randomized phase 2 study of apalutamide with or without stereotactic body radiation to PSMA PET-avid sites of disease in oligometastatic CRPC” (National PI: Rahul Aggarwal). Participating sites within the PCCTC include UCLA (PI: Matt Rettig) and the University of Wisconsin (PI: Glenn Liu). The study is expected to open to accrual at UCSF in Q4 2019, and participating sites in the first half of 2020.

UCSF is currently in the process of activating four additional PCCTC clinical trials led by other institutions within the PCCTC, including the following:

1) COMbination of Bipolar Androgen Therapy and Nivolumab in Patients with Metastatic Castration-Resistant Prostate Cancer (COMBAT-CRPC)– Lead Investigational Site: Johns Hopkins University; UCSF PI: Rahul Aggarwal

2) A Phase II Combination Trial of the PI3K-β Selective Inhibitor GSK2636771 with Pembrolizumab for PTEN-deficient Metastatic Castrate-Resistant Prostate Cancer and Metastatic Endometrial Cancer Patients: Lead Investigational Site: U of Chicago; UCSF PI: Rahul Aggarwal

3) IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations; Lead Investigational Site: U of Michigan; UCSF PI: Eric Small

4) 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

The activation of these trials will help to boost UCSF accrual to PCCTC studies led by other institutions within the consortium.

4. Impact

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

Tom Hope and colleagues at UCSF have published the prospective trial results of Ga-PSMA-11 PET imaging in patients with serologically relapsed prostate cancer (see list of publications). The results of this study have supported the development of an accepted PCCTC multi-center, investigator-initiated randomized phase 2 trial of apalutamide with or without SBRT in oligometastatic CRPC by PSMA PET.

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. Changes/Problems. The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

We have encountered slight delays in finalizing the budget and contract for the activation of several PCCTC trials led by other institutions, which has impacted our accrual to non-UCSF PCCTC trials. Trials in activation include:

1) COMbination of Bipolar Androgen Therapy and Nivolumab in Patients with Metastatic Castration-Resistant Prostate Cancer (COMBAT-CRPC)– Lead Investigational Site: Johns Hopkins University; UCSF PI: Rahul Aggarwal

2) A Phase II Combination Trial of the PI3K-β Selective Inhibitor GSK2636771 with Pembrolizumab for PTEN-deficient Metastatic Castrate-Resistant Prostate Cancer and Metastatic Endometrial Cancer Patients: Lead Investigational Site: U of Chicago; UCSF PI: Rahul Aggarwal

3) IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations; Lead Investigational Site: U of Michigan; UCSF PI: Eric Small

4) 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

We are working with the UCSF Cancer Center Investigational Trials Resource (ITR) to identify methods to speed up the process of trial activation. As part of a pilot program, the UCSF PI (Rahul Aggarwal) has a dedicated budget analyst assigned for the development of budgets that will facilitate trial activation.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

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,** 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

2. Quigley DA, Dang HX, Zhao SG, Lloyd P, **Aggarwal R**, Alumkal JJ, Foye A, Kothari V, Perry MD, Bailey AM, Playdle D, Barnard TJ, Zhang L, Youngren JF, Cieslik MP, Parolia A, Beer TM, Thomas G, Chi KN, Gleave M, Lack NA, Zoubeidi A, Reiter RE, Rettig MB, Witte O, Ryan CJ, Fong L, Kim W, Friedlander T, Chou J, Li H, Das R, Li H, Moussavi-Baygi R, Goodarzi H, Gilbert LA, Lara PN, Evans CP, Goldstein TC, Stuart JM, Tomlins SA, Spratt DE, Cheetham RK, Cheng DT, Farh K, Gehring JS, Hakenberg J, Liao A, Febbo PG, Shon J, Sickler B, Batzoglou S, Knudsen KE, He HH, Huang J, Wyatt AW, Dehm SM, Ashworth A, Chinnaiyan AM, Maher CA, **Small EJ**, and Feng FY. Genomic hallmarks and structural variation in metastatic prostate cancer. Cell 2018; 174:758-69. PMID 30033370.

3. Su Y, Liu Y, Behrens CR, Bidlingmaier S, Lee N, **Aggarwal R**, Sherbenou DW, Burlingame AL, Hann BC, Simko JP, Premasekharan G, Paris PL, Shuman MA, Seo Y, **Small EJ**, Liu B. Targeting CD46 for both adenocarcinoma and neuroendocrine prostate cancer. Journal of Clinical Investigation Insight [in press; accepted for publication 24 July 2018].

4. **Aggarwal R**, Quigley D, Huang J, Zhang L, Beer T, Rettig M, Reiter R, Gleave M, Thomas G, Foye A, Playdle D, Lloyd P, Chi K, Evans CP, Lara P, Feng FY, Alumkal J, and **Small EJ**. Whole genome and transcriptional analysis of treatment-emergent small cell neuroendocrine prostate cancer demonstrates intra-class heterogeneity. Molecular Cancer Research [in press; accepted for publication 11 Mar 2019].

5. Chen WS, **Aggarwal R**, Zhang L, Zhao SG, Thomas GV, Beer TM, Quigley DA, Foye A, Playdle D, Huang J, Lloyd P, Lu E, Sun D, Guan X, Rettig M, Gleave M, Evans CP, Youngren J, True L, Lara P, Kothari V, Xia Z, Chi KN, Reiter RE, Maher CA, Feng FY, **Small EJ**, and Alumkal JJ. Genomic drivers of poor prognosis and enzalutamide resistance in metastatic castration-resistant prostate cancer. European Urology [in press; accepted for publication 13 Mar 2019].

6. **Aggarwal R**, Abida W, Schweizer M, Pantuck A, Nanus D, Heath E, Lakhotia S, Hansen H, Silverman M, Bauman L, Snyder M, Campeau E, Norek K, Attwell S, O'Farrell M, Smith S, Wegge P, Jahagirdar R, 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. AACR Annual Meeting 2019, Atlanta, GA, USA.

7. 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.

7. Participants and Other Collaborating Organizations

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

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?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed. Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other*

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 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: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

SUPPORTING DATA:
University of California, San Francisco
Table A. Trials Introduced by UCSF (as of 09/30/2019)
Table B. Patient Accrual by UCSF (09/30/2018 – 09/30/2019)

Table A. Trials Introduced by UCSF (As of 09/30/2019)

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	23	04/28/2015	9/25/2015	N/A	**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	N/A	**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	8	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	N/A	**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	8	12/13/2018	2/4/2019	N/A	**OHSU, UCLA, Northwestern, Karmanos**

Table B. Accrual in Reporting Period

PCCTC #	Lead Institution	Study Title	Patient Accrual Between 9/30/2018 - 03/30/2019	Patient Accrual Between 4/1/2019 – 10/1/2019	Total Accrual Between 9/30/2018 – 10/1/19
c15-149	UCSF	Tax/LEE	6	5	11
c15-166	UCSF	Zen/Enza	9	1	10
c18-221	UCSF	FOR46	3	5	8
c15-160	MSKCC	CC-115 + Enzalutamide	2	1	3
Total Accrual			**20**	12	32