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TITLE: **Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC)**

PRINCIPAL INVESTIGATOR: Ana Aparicio, M.D.

CONTRACTING ORGANIZATION: The University of Texas MD Anderson Cancer Center
Houston, TX

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Ana Aparicio, MD

E-Mail: aaparicio@mdanderson.org

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The University of Texas
MD Anderson Cancer Center
1515 Holcombe Boulevard
Houston, TX 77030-4009

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14. ABSTRACT

Men with androgen indifferent prostate cancers have a dismal prognosis and limited treatment options. To provide a framework for their study and therapy development, we defined the ***aggressive variant prostate cancers*** (AVPC) and in previous studies obtained evidence that men with AVPC benefit from the addition of carboplatin to cabazitaxel chemotherapy, and likely from PARP inhibitor maintenance following chemotherapy induction. Building on this work and based on the evidence of immune-modulation by chemotherapy and PARP inhibitors in preclinical studies, as well as the clinical benefit observed with the addition of immune-checkpoint therapy to chemotherapy in patients with aggressive malignancies that share similarities with the AVPC, we **hypothesized that PD-1 inhibition will enhance the anti-tumor response of platinum-based chemotherapy induction and PARP inhibitor maintenance in men with AVPC.** To test this hypothesis, we proposed this phase II randomized trial in which men with AVPC are treated with up to 6 cycles of cabazitaxel-carboplatin induction, with the anti-PD1 inhibitor cetrelimab added on Cycle #2 of treatment, and then randomized to the PARP inhibitor niraparib vs niraparib plus cetrelimab maintenance. Tumor biopsies are mandated at 3 timepoints. Our primary objectives are to estimate the progression free survival of men with AVPC in each arm and evaluate the changes in the density and localization of immune markers and cell subsets in tumor biopsies. The study was activated on 12/29/2020. As of 09/16/2021, 23 patients have been registered and 28 tissue samples have been assembled.

15. SUBJECT TERMS

Prostate cancer, aggressive variant prostate cancers, small cell or neuroendocrine prostate carcinomas, immunotherapy, chemotherapy, carboplatin, cabazitaxel, olaparib, durvalumab, PD-L1

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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13. SUPPLEMENTARY NOTES

TABLE OF CONTENTS

1. INTRODUCTION

The purpose of this study is to determine the effect of anti-PD1 inhibition (cetrelimab) on the efficacy and immune-modulatory effects of cabazitaxel-carboplatin induction chemotherapy and PARP inhibitor (niraparib) maintenance therapy in men with *aggressive variant prostate cancers* (AVPC).
Up to 120 men with AVPC will be treated with up to 6 cycles of cabazitaxel-carboplatin chemotherapy, to which cetrelimab will be added on cycle 2, in order to randomize 88 to maintenance therapy with niraparib with or without cetrelimab. Tumor biopsies are obtained after cycle 1 (before the addition of cetrelimab), after cycle 3 (once 2 cycles with the combination of chemotherapy and cetrelimab have been completed) and then, after 3 cycles of niraparib with or without cetrelimab are complete. Efficacy will be determined based on progression free survival, and multiplex immunofluorescence will be used to identify PD-L1, CD4, CD8, CD68 and CD163 expression in tumor biopsies.

2. KEYWORDS:

Prostate cancer, aggressive variant prostate cancers, small cell or neuroendocrine prostate carcinomas, immunotherapy, chemotherapy, carboplatin, cabazitaxel, niraparib, cetrelimab, PD1

3. ACCOMPLISHMENTS

What were the major goals of the project?

Major Tasks:

1. Prepare for Clinical Trial Activation
   Milestone: *Clinical trial ready for activation*
   - **Expected, 09/2020**
   - **Completed, 12/2020 (Funding activated at The University of Texas MD Anderson Cancer Center 01/15/2021)**
2. Participant Recruitment, Treatment and Evaluation
   Milestone 1. *1st participant consented, screened and enrolled*
   - **Expected, 10/2020**
   - **Completed, 01/2021**

   Milestone 2. *Complete accrual (88-120 patients)*
   - **Expected, 04/2022**
   - **Ongoing, n=23 patients registered to date, 20% of planned accrual**

   Milestone 3. *Complete toxicity and efficacy evaluations*
   - Expected, 10/2023
   - Ongoing
3. Sample Collection and Distribution
   Milestone 1. *Complete sample collection (88-120 patients)*

- **Expected, 10/2023**
- **Ongoing**
  Biopsy # 1 (post-cycle #1 cabazitaxel-carboplatin) obtained from n=18 patients to date.
  Biopsy #2 (post-cycle #3 cabazitaxel-carboplatin-cetrelimab) obtained from n=10 patients to date.

4. Multiplex IF Analysis and Interpretation
   Milestone 1. *Complete multiplex IF analysis and interpretation*
   - Expected, 03/2024
   - Awaiting collection of complete biopsy set (biopsies 1, 2 and 3) from first 12 patients to begin analyses

5. Single-cell RNA sequencing *Note: Funding not included in this award.*
   Milestone 1. *Complete interim analysis of sc-RNA-seq*
   - Expected, 09/2021
   - Awaiting collection of complete biopsy set (biopsies 1, 2 and 3) from first 12 patients to begin analyses

   Milestone 2. *Complete scRNA-seq and interpretation*
   - Expected 03/2024
   - Awaiting collection of complete biopsy set (biopsies 1, 2 and 3) from first 12 patients to begin analyses

6. Data Analysis, Dissemination and Manuscript Preparation
   Milestone 1. *Complete assembly of clinical data*
   - Expected, 12/2023
   - Pending trial completion

   Milestone 2. *Complete statistical analysis of clinical endpoints*
   - Expected 03/2024
   - Pending trial completion

   Milestone 3. *Integrate clinical and correlative data*
   - Expected, 06/2024
   - Pending trial completion

   Milestone 4. *Report of findings in abstract form*
   - Expected, 07/2024
   - Pending trial completion

   Milestone 5. *Final report*
   - Expected 09/2024
   - Pending trial completion

What was accomplished under these goals?

Astra Zeneca ultimately declined to provide durvalumab and olaparib but we were able to procure support from Janssen (provision of cetrelimab and niraparib) to conduct this trial. Clinical trial activation was delayed by 3 months while negotiations and protocol amendments were reviewed. Starting in 01/2021, accrual has ranged from 1 to 6 patients per month, average 2.75/month. This is

slightly below our originally expected accrual of 4/month but is above expectations in the context of the COVID19 pandemic.

We have successfully obtained the following tumor samples for correlative studies:

- Biopsy # 1 (post-cycle #1 cabazitaxel-carboplatin)

Collected from n=18 patients to date. Of these, 1 collection occurred after cycle 2 had been administered due to a scheduling error and 1 collection consisted only of a FNA (the lesion was too small to obtain additional cores safely). An additional 3 are pending (timepoint not reached). Two patients were removed from study before the biopsy timepoint (one declined participation after signing consent and the other was diagnosed with an intercurrent illness that precluded his return for follow-up).

- Biopsy #2 (post-cycle #3 cabazitaxel-carboplatin-cetrelimab)

Collected from n=10 patients to date. Of these, 1 collection consisted only of a FNA (lesion too small to obtain cores safely), 1 collection was aborted as the lesion had disappeared, and 1 occurred after cycle #4 was administered due to a scheduling error. An additional 7 are pending (timepoint not reached). Three patients did not undergo biopsy #2, one due to intercurrent illness, and 2 due to disease progression.

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

Nothing to Report

How were the results disseminated to communities of interest?

Nothing to report.

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

Continue accrual and tumor biopsy assembly. We expect the 12th patient to have reached the 3rd biopsy timepoint by 01/13/2022 at which time we will subject an initial set of biopsies for multiplex immunofluorescence and single-cell RNA sequencing.

4. IMPACT

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

Nothing to report.

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

As detailed above, activation was delayed by 4 months and, in the context of the COVID19 pandemic, accrual has been slightly below our original expectation, at approximately 3 patients/month on average, instead of 4 patients/month as originally proposed. Hence we are at 20% of accrual, instead of the expected 40%. Nonetheless, accrual has been robust during the most recent months and we expect to complete accrual by Year 3, as proposed.

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

Two changes from the original proposal have been implemented, following approval by the DoD, as well as the MD Anderson IND Office and IRB:

1. As detailed above, the immune-checkpoint inhibitor cetrelimab and the PARP inhibitor niraparib (provided by Janssen) were substituted for the immune-checkpoint inhibitor durvalumab and the PARP inhibitor olaparib (Astra Zeneca) that were included in the original proposal. These changes did not affect the endpoints of our study given the similarities between the drugs.

2. We have modified the eligibility criteria to allow:

    a. Biopsy proven *new* transformation to small cell carcinoma in a patient previously diagnosed with an adenocarcinoma of the prostate' as evidence of progressive disease.
    b. Prior treatment with an anti-PD1 or anti-PDL1 inhibitor, contingent on PI approval, as long as it was administered in monotherapy or in combination with drugs whose mechanism of action does not overlap with that of the other drugs used in the study (e.g. docetaxel) and the patient did not experience an immune-related adverse event (irAE) that led to the permanent discontinuation of prior immunotherapy.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations. Nothing to report.

- **Website(s) or other Internet site(s)**

  Nothing to report.

- **Technologies or techniques**

  Nothing to report.

- **Inventions, patent applications, and/or licenses**

  Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	**Ana Aparicio**
Project Role:	Principal Investigator
Research Identifier (e.g. ORCID ID):	000-0003-0900-0923
Nearest Person Months Worked:	1 calendar month
Contribution to Project:	Dr. Aparicio supervises all aspects of the proposed work and leads the clinical study.
Funding Support:	N/A

Name:	**James P. Long**
Project Role:	Statistician
Research Identifier (e.g. ORCID ID):	0000-0001-5853-5938
Nearest Person Months Worked:	1 calendar month
Contribution to Project:	Dr. Long supervises the monitoring of the trial, as well as the statistical analysis of the clinical trial outcomes and that of the correlative data.
Funding Support:	N/A

Name:	**Rebecca Slack Tidwell**
Project Role:	Sr. Statistical Analyst
Research Identifier (e.g. ORCID ID):	0000-0003-3041-8582
Nearest Person Months Worked:	1 calendar month
Contribution to Project:	She has contributed the statistical design of this proposal and will assist in the statistical analysis of the clinical trial outcomes, as well as the correlative data, for interpretation and publication.
Funding Support:	N/A

Name:	**Mercedes Villareal**
Project Role:	Clinical Trial Oversight Coordinator
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	2 calendar months
Contribution to Project:	She oversees data entry, performs quality control audits and assists in the preparation of data summaries for communication with regulatory agencies and supporting companies (e.g. accrual updates, AE reports and continuing reviews).
Funding Support:	N/A

Name:	**Tamatha Godine**
Project Role:	Correlative Studies Research Coordinator
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	3 calendar months
Contribution to Project:	She is responsible for monitoring the assembly and distribution of biological samples obtained from study participants, coordination of data analysis and integration, generation of data figures and tables for presentation.
Funding Support:	N/A

Name:	**Stacy Harris**
Project Role:	Research Nurse, from September-November 2020
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	2 calendar months
Contribution to Project:	She assisted Dr. Aparicio with the screening and follow up of patients.
Funding Support:	N/A

Name:	**Erica Frankel**
Project Role:	Research Nurse, 20% from December 2020-February 2021
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	2 calendar months
Contribution to Project:	She assisted Dr. Aparicio with the screening and follow up of patients.
Funding Support:	N/A

Name:	**Collin Wehunt**
Project Role:	Research Nurse effective March 2021-present
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	4 calendar months
Contribution to Project:	Collin assists Dr. Aparicio with the screening and follow up of patients.
Funding Support:	N/A

Name:	**Rosalin Mouton**
Project Role:	Data Entry Staff
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	1 calendar month
Contribution to Project:	Ms. Mouton assists in procuring data elements from outside facilities (e.g. safety laboratory studies) and is responsible for data entry into the Prometheus Software Platform.
Funding Support:	N/A

Name:	**Leena Abraham**
Project Role:	Regulatory Oversight Coordinator
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	2 calendar months
Contribution to Project:	Ms. Abraham works with the Trial Oversight Coordinator to maintain the schedule of communications with regulatory agencies and is responsible for the submission of the required documentation to such agencies. This includes submission of any required amendments and supervision of appropriate filing of all required regulatory documentation.
Funding Support:	N/A

Name:	**Glenda Myers**
Project Role:	Tissue Procurement Specialist
Research Identifier (e.g. ORCID ID):	N/A
Nearest Person Months Worked:	1 calendar month
Contribution to Project:	Ms. Myers is responsible for the collection, procurement and harvest of fresh biological specimens mandated during study conduct and requested (optional) at end of treatment; facilitating specialized harvests for investigators; and processing, archiving and distribution of routine specimens banked for future use. She also assists in the reconciliation

	and organization of data and records for timely submission of reports on the procured human tissues.
Funding Support:	N/A

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

APARICIO, Ana

CURRENT

NCT03263650	*(Aparicio)*
Title:	*2017-0133: Randomized Phase II Study of Olaparib Maintenance Following Cabazitaxel-Carboplatin Induction Chemotherapy in Men with Aggressive Variant Prostate Cancer (AVPC)*
Time Commitments:	0.12 calendar months (1% effort)
Supporting Agency:	AstraZeneca
Grants Officer:	Gayle Ewing, Gayle.Ewing@astrazeneca.com
Performance Period:	08/15/2017-08/14/2022
Level of Funding:	
Goal(s):	The goal of this clinical research study is to learn if olaparib, when given after treatment with cabazitaxel, carboplatin, and prednisone, can help to control aggressive variant prostate cancer (AVPC). The safety of these drugs will also be studied.
Specific Aims:	Same as above
Role:	Principal Investigator
Overlap:	None

(This grant was granted a no-cost extension to 8/31/2022)

P50 CA140388-10	*(Logothetis/Thompson)*
Title:	*MD Anderson Cancer Center Prostate Cancer SPORE Project 1: Integrating Ipilimumab Immunotherapy with Approved Treatment Strategies in CRPC*
Time Commitments:	0.36 calendar months (3% effort)
Supporting Agency:	NIH/NCI
Grants Officer:	Ashley Salo, 240-276-5656, ashley.salo@nih.gov
Performance Period:	09/01/2016-08/31/2022 NCE
Level of Funding:	
Goal(s):	To rationally integrate anti-CTLA-4 (ipilimumab) immunotherapy with agents targeting the AR signaling pathway to provide durable clinical benefit with improved survival in patients with prostate cancer, and utilize novel imaging techniques to accurately identify tumor responses.
Specific Aims:	1. To identify biological changes indicative of mechanistic pathways that contribute to clinical outcomes in matched tumor and blood specimens obtained from prostate cancer patients given drugs targeting the AR signaling pathway plus anti-CTLA-4 immunotherapy. 2. To determine clinical outcomes after treatment with AR-targeting

	agents (ARN-509 + abiraterone acetate) followed by concurrent anti-CTLA-4 immunotherapy and prospectively evaluate the effectiveness of selected biological pathways identified in Aim 1 to be indicative of mechanistic pathways that contribute to clinical outcomes. 3. To determine the efficacy of targeting B7-H3 and B7-H4 with radiolabeled monoclonal antibodies as a non-invasive means to detect prostate cancer.
Role:	Co-Investigator, Project 1
Overlap:	None

(NEW)

Prostate Moon Shot	*(Logothetis)*
Title:	*Prostate Cancer Moon Shot* *Project 2: An Integrated Definition and Therapeutic Strategy for Androgen Indifferent Prostate Cancers*
Time Commitment:	0 calendar months, unsalaried
Supporting Agency:	MD Anderson Moon Shot Program
Grants Officer:	Carrie C. Feighl, 713-792-3477, research_finance@mdanderson.org
Performance Period:	09/01/2021-08/31/2022
Level of Funding:	annual direct
Goal(s):	To develop effective therapies for the androgen indifferent prostate cancers, a subset with dismal prognosis and very limited treatment options.
Specific Aims:	1. To stratify the AVPC based on integrated genomic and tumor compartment-specific transcriptomic signatures across prospective clinical trials spanning the natural history of advanced prostate cancers. 2. To determine the effects of valemetostat and cabazitaxel-carboplatin on the epithelial and immune compartments of AVPC tumors.
Role:	Project Lead
Overlap:	None

NCT02703623	*(Aparicio)*
Title:	*2014-0386: A Dynamic Allocation Modular Sequential Trial of Approved and Promising Therapies in Men with Metastatic Castrate Resistant Prostate Cancer*
Time Commitments:	0.12 calendar months (1% effort)
Supporting Agency:	Janssen Pharmaceuticals Inc.
Performance Period:	05/03/2016-05/02/2024
Level of Funding:	
Goal(s):	This randomized phase II trial studies the side effects and how well abiraterone acetate, prednisone, and apalutamide work with or without ipilimumab or cabazitaxel and carboplatin in treating patients with castration-resistant prostate cancer that has spread to other places in the body.
Specific Aims:	1. Estimate the overall survival (OS) of men with metastatic castration-resistant prostate cancer (mCRPC) who have satisfactory features after to 8 weeks of maximal androgen receptor (AR)-inhibitory therapy and receive treatment with abiraterone acetate, prednisone and apalutamide plus or minus ipilimumab.

	2. Estimate the OS of men with mCRPC who have unsatisfactory features after to up to 8 weeks of maximal androgen receptor (AR)-inhibitory therapy and receive treatment with abiraterone acetate, prednisone, apalutamide, cabazitaxel and carboplatin. 3. Determine the toxicity profile of the following combinations in men with mCRPC: a. Abiraterone acetate, prednisone, apalutamide. b. Abiraterone acetate, prednisone, apalutamide and ipilimumab. c. Abiraterone acetate, prednisone, apalutamide, cabazitaxel and carboplatin. 4. Determine whether the baseline "AR response signature" correlates with satisfactory or unsatisfactory features after up to 8-weeks of treatment with abiraterone, prednisone and apalutamide.
Overlap:	None
(THIS AWARD)	
W81XWH-20-10257	*(Aparicio)*
Title:	*PC190353: Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC)*
Time Commitments:	1.20 calendar months (10% effort)
Supporting Agency:	DOD
Grants Officer:	Kenneth E. Grenier, 301-619-2728, kenneth.e.grenier2.civ@mail.mil
Performance Period:	09/01/2020-08/31/2024
Level of Funding:	
Goal(s):	Our overall goal is to arrive at biologically-based rational combinations to treat the AVPC with curative intent.
Specific Aims:	1. Determine the effect of durvalumab on the clinical efficacy of cabazitaxel-carboplatin induction and olaparib maintenance in men with AVPC. 2. Determine the effects of durvalumab on the immune components of the tumor microenvironment when added to cabazitaxel-carboplatin induction and to olaparib maintenance in men with AVPC.
(NEW)	
W81XWH-21-1-0522	*(Wang)*
Title:	*PC200420: Targeting Histone Lysine Demethylase KDM4A in Neuroendocrine Prostate Cancer*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	DOD
Grants Officer:	Kimberly Carter, 301-619-2249, Kimberly.m.carter47.civ@mail.mil
Performance Period:	09/01/2021-08/31/2024
Level of Funding:	
Goal(s):	Our overall goal is to develop combination therapy to improve the clinical outcome of platinum-taxane chemotherapy in patients with NEPC.
Specific Aims:	1. Determine the role of KDM4A in NEPC progression using organoids, PDXs, and GEMMs. 2. Examine the mechanism(s) by which KDM4A regulates UPR signaling. 3. Determine whether KDM4 inhibitors improve the therapeutic outcomes of platinum-taxane chemotherapy in NEPC.
Role:	Co-Investigator
Overlap:	None

(NEW)

NCT04388852	*(Aparicio)*
Title:	*2019-0967: DS3201 With Ipilimumab in Patients with Metastatic Aggressive Variant Prostate (AVPC), Urothelial (UC), and Renal Cell (RCC) Carcinomas*
Time Commitments:	0 calendar months
Supporting Agency:	MD Anderson
Performance Period:	03/18/2020-no end date (End date will be when study is completed)
Level of Funding:	
Goal(s):	This phase Ib trial studies the side effects and best dose of DS3201 when given together with and ipilimumab for the treatment of patients with prostate, urothelial, or renal cell cancer that has spread to other places in the body (metastatic). DS3201 may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. Immunotherapy with monoclonal antibodies, such as ipilimumab, may help the body's immune system attack the cancer, and may interfere with the ability of tumor cells to grow and spread. Giving DS3201 and ipilimumab may help to control the disease.
Aims:	Primary objectives: 1. Determine the maximum tolerated dose (MTD) and confirm the safety and tolerability of valemetostat (DS3201) given in combination with ipilimumab in patients with metastatic aggressive variant prostate cancers (AVPC), urothelial carcinomas (UC) and renal clear cell carcinomas (RCC). 2. Screen for associations between changes in the tumor microenvironment and clinical outcomes. Secondary objectives: 1. To assess the immunologic and molecular effects on tissue samples of participants treated with DS3201 in combination with ipilimumab in patients with metastatic AVPC, UC and RCC. 2. To estimate the time to treatment failure (TTF) of patients with metastatic AVPC, UC and RCC treated with DS3201 in combination with ipilimumab. 3. To estimate the overall response rate (ORR) of patients with metastatic AVPC, UC and RCC treated with DS3201 in combination with ipilimumab (in patients with AVPC ORR will be reported separately for prostate specific antigen [PSA], circulating tumor cells [CTC] and measurable and non-measurable disease by Response Evaluation Criteria in Solid Tumors [RECIST] 1.1).
Overlap:	None

PREVIOUS (Recently completed)

Prostate Moon Shot	*(Giancotti/Logothetis)*
Title:	*Prostate Cancer Moon Shot. Flagship 1: Epithelial Plasticity and Mechanisms of Resistance and Progression in AVPC*
Time Commitments:	0.60 calendar months (5% effort), unsalaried
Supporting Agency:	MD Anderson Moon Shot Program
Grants Officer:	Carrie C. Feighl, 713-792-3477, research_finance@mdanderson.org
Performance Period:	09/01/2019-08/31/2020
Level of Funding:	
Goal(s):	To elucidate the origin and define the vulnerabilities of AVPC to develop effective mechanism-based therapies for this substantial fraction of metastatic castration-resistant prostate cancer.

Specific Aims:	1. To define molecular biomarkers that identify AVPC in patients and preclinical models. 2. To identify biologically and clinically relevant subsets of AVPC based on evolutionary trajectories and oncogenic mutations. 3. To define therapeutically relevant drivers and vulnerabilities in AVPC and its subsets. 4. To test the efficacy of mechanism-based therapies targeting AVPC tumor cells and their immune microenvironment.
Role:	Co-PI, Flagship 1
Overlap:	None

Emerson	*(Goswami)*
Title:	*Epigenetic Modulation with EZH2 Inhibition Can Overcome Resistance to Immune Checkpoint therapy*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	Emerson Collective
Grants Officer:	Carrie C. Feighl, 713-792-3477, research_finance@mdanderson.org
Performance Period:	11/01/2018-10/31/2020
Level of Funding:	
Goal(s):	This study will serve to support our overall hypothesis that epigenetic modulation with EZH2 inhibition can overcome resistance to immune checkpoint therapy by enhancing T-cell mediated antitumor immunity and immunogenic tumor cell intrinsic pathways. We will test our hypothesis with two specific aims.
Specific Aims:	1. To interrogate the cellular subpopulations in the tumor microenvironment and the peripheral blood of patients with immune checkpoint-refractory genitourinary malignancies at baseline, and following treatment with CPI-1205 alone and with CPI-1205+Ipilimumab. 2. To determine the changes induced by treatment with the EZH2 inhibitor CPI-1205, alone and in combination with the CTLA-4 inhibitor Ipilimumab, on the chromatin profiles of immune cell populations in the peripheral blood of patients with immune checkpoint-refractory genitourinary malignancies.
Role:	Co-Principal Investigator
Overlap:	None

LONG, James

CURRENT

(Received a no-cost extension to 08/31/2021)

P50 CA140388-10	*MD Anderson Cancer Center Prostate Cancer SPORE. Core 1: Biostatistics Core (Logothetis/Thompson)*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	NIH/NCI
Grants Officer:	Ashley Salo, Grants Management Specialist, ashley.salo@nih.gov
Performance Period:	09/01/2016-08/31/2022
Level of Funding:	
Goal(s):	The Biostatistics and Bioinformatics Core provides comprehensive biostatistic and bioinformatic expertise to ensure statistical integrity and

optimize data analysis for the studies in the SPORE. (Effort ended effective 9/1/2021)

Specific Aims:
1. Provide guidance in the design and conduct of clinical trials and other experiments (including high-dimensional genomic and proteomic studies) that arise from the ongoing research of the SPORE.
2. Provide innovative and tailored statistical modeling, simulation techniques, and data analyses as needed for the main projects, developmental research and career development projects, and other cores to achieve their specific aims.
3. Ensure that the results of all projects are based on well-designed experiments and are appropriately interpreted.
4. Provide guidance in the design and use of an information system to store appropriate data generated by all projects; develop integrated computational libraries and tools for producing documented, reproducible statistical and bioinformatics analyses; and support the use of these tools for analyses conducted by and on behalf of the projects.

Role: Co-Investigator
Overlap: None

5 P30 CA016672-45 *Cancer Center Support Grant (CCSG)-Biostatistics Resource Group (Pisters)*
Time Commitments: 1.20 calendar months (10% effort)
Supporting Agency: NIH/NCI
Grants Officer: Ogunbiyi, Peter ogunbiyip@mail.nih.gov
Performance Period: 08/28/1996-06/30/2024
Level of Funding:
Goal(s): To enhance the scientific excellence of research at MD Anderson through outstanding statistical designs and methods, including the proper and efficient use of standard and cutting-edge methods.

Specific Aims:
1. Provide statistical collaboration and consultation services in support of cancer research in laboratory experiments and clinical trials;
2. Play a direct role in the planning and review of clinical protocols;
3. Provide educational programs in biostatistical methods; and
4. Design, develop, distribute, and implement software and database systems to support all the computational needs of cancer researchers.

Role: Biostatistician
Overlap: None

R01 CA218004 *Translational Applications in an Animal Model of Pancreatic Cystic Neoplasm and Cancer (Maitra)*
Time Commitments: 4.25%, 0.51 calendar months
Supporting Agency: NIH/NCI
Grants Officer: Walters, Angela, Phone: 240-276-5351, angela.walters@nih.gov
Performance Period: 04/04/2018-03/31/2022
Level of Funding:
Goal(s): To address key unmet needs in the management of IPMNs in three areas: imaging correlates, circulating biomarkers, and precision immunotherapy. PID6462

Specific Aims: 1. Use the animal model to investigate two novel imaging platforms – quantitative feature extraction from MRI scans using an indigenously developed algorithm known as "Enhancement Pattern Mapping" (EPM) and second, hyperpolarized MRI (HPMRI), in order to determine imaging correlates that coincide with the transition from low grade IPMN to cancer.
2. Use a combination of unbiased mass spectrometry and array-based approaches to identify circulating proteins and autoantibodies that correlate with progression of murine IPMNs to PDAC. Both aims will benefit from access to MRI scans and biospecimens from IPMN patients for validation studies, through NCI-funded multicenter U01 consortia that are led by the PI.
3. Attempt immunoprevention of PDAC progression to IPMNs, using a multivalent peptide vaccine generated by comprehensive mapping of tumor epitopes in Kras;Gnas mice.

Role: Co-Investigator
Overlap: None

The Transformative Glioblastoma Initiative (Heimberger)
Time Commitments: 2.69 calendar months (22.43%)
Supporting Agency: Brockman Foundation
Grants Officer: Stuart C. Yudofsky Suite 539, 48 Par-la-Ville Road, Hamilton HM11, Bermuda
Performance Period: 12/11/2018-12/10/2021
Level of Funding:
Goal(s): To design therapeutic strategies that can overcome tumor heterogeneity in GBM.
Specific Aims: Provide bio statistical expertise and quantitative research resources in support of all of the eight projects in this grant.
Role: Co-Investigator
Overlap: None

(NEW)
U01 CA239522-01A1 *Longitudinal Proteomic and Metabolomic Predictors of Pancreatic Cyst Malignant Progression and Early Stage Pancreatic Cancer (Schmidt)*
Time Commitments: 0.60 calendar months (5% effort)
Supporting Agency: NIH/NCI subaward via Indiana University
Grants Officer: Claire Zhu, cz63u@nih.gov
Performance Period: 04/01/2021-03/31/2026
Level of Funding:
Goal(s): To identify and validate protein and metabolite signatures and their longitudinal changes which can discriminate IPMN malignant progression and detect early-stage PDAC.
Specific Aims: 1. Investigate plasma and cyst fluid levels and trajectories of proteomic biomarkers and metabo-lomics signatures for prediction of IPMN malignant progression in a prospective surveillance cohort.
2. Evaluate levels and trajectories of plasma proteomic biomarkers and metabolomics signatures for detection of early-stage PDAC in a PRoBE-compliant case-control study nested in the PLCO cohort.

Role:	Co-Investigator
Overlap:	None
R01 CA231465-02	*Rigorous and Reproducible Mutational Analysis of the Urinary Exosomal DNA/ (Dinney/Kalluri)*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	NIH/NCI
Grants Officer:	Matthew R. Young, 240-276-5846, youngma@mail.nih.gov
Performance Period:	07/1/2019-06/30/2024
Level of Funding:	
Goal(s):	To test the utility of exoDNA as an analyte, for detection, and monitoring of bladder cancer as well as identification of novel drivers and pathways that contribute to BLCA progression. PID8079
Specific Aims:	1. Identify procedure(s) to obtain high quality exosomes and maximize exoDNA yield from urine. 2. Optimize whole genome amplification of serum and urine exoDNA. 3. Determine computational procedures for rapid and reproducible identification of mutations and biomarkers using exoDNA. 4. Independent validation of exoDNA analysis in bladder cancer.
Role:	Co-Investigator
Overlap:	None
(NEW)	
5 UL1 TR003167-03	*Center for Clinical and Translational Science (Karp)*
Time Commitments:	1.20 calendar months (10% effort)
Supporting Agency:	NIH/NCATS subaward via UT Health Science Center, Houston
Grants Officer:	Carol Merchant, 301-435-0605, merchantc@mail.nih.gov
Performance Period:	07/24/2019-06/30/2024
Level of Funding:	
Goal(s):	This program advances clinical and translational science and maximizes the speed at which novel treats can be brought to patients to improve outcomes and quality of life.
Specific Aims:	1. Provide our investigators, staff, trainees, and scholars with the skills and knowledge necessary to advance discoveries and their translation in the new environment of clinical and translational research (Workforce Development). 2. Collaborate with all of our stakeholders in a mutually beneficial way to advance translation by furthering engagement and team science (Collaboration/Engagement). 3. Integrate pediatric and geriatric patients, Hispanic patients with cancer, and the LGBTQ+ community into the full spectrum of clinical and translational research (Integration). 4. Advance translational science by providing novel processes, increasing efficiency, and streamlining research (Methods/Processes). 5. Create and apply innovative informatics solutions to advance translational research, train the CTSA workforce, disseminate best practices, engage communities and integrate clinical and basic research data (Informatics).
Role:	Collaborator

Overlap: None

P50 CA127001-12 *SPORE in Brain Cancer (Lang)*
Time Commitments: 1.20 calendar months (10% effort)
Supporting Agency: NIH/NCI
Grants Officer: Leah Hubbard, 240-276-5693, leah.hubbard@nih.gov
Performance Period: 09/01/2019-08/31/2023
Level of Funding:
Goal(s): To conduct cutting-edge translational research for the prevention and treatment of brain cancer.
Specific Aims: 1. Provide biostatistics and bioinformatics expertise in the design and conduct of laboratory experiments and clinical trials arising from the research proposed in this application.
2. Provide biostatistics and bioinformatics analysis and interpretation of all data collected under the SPORE Projects, Developmental Projects, and other Cores.
3. Collaborate and assist all project investigators with the publication of scientific results.
Role: Co-Investigator
Overlap: None

(NEW)
5 R01 DE029590 *Precision Optical Guidance for Oral Biopsy Based on Next-Generation Hallmarks of Cancer (Gillenwater)*
Time Commitments: 0.3 calendar months (2.5% effort)
Supporting Agency: NIH/NIDCR Subaward Rice University
Grants Officer: Amanda Melillo, 301-827-4647, amanda.melillo@nih.gov
Performance Period: 02/25/2020-01/31/2025
Level of Funding:
Goal(s): To develop and validate a multimodal Active Biopsy Guidance imaging system that provides precise biopsy guidance for detection of oral neoplasia based on the next generation of hallmarks of cancer. (Effort effective 9/1/2020) PID11276
Specific Aims: 1. Develop a compact optical mapping scope that uses Digital Light Processing (DLP) technology to image tissue autofluorescence and actively project a map onto the tissue that highlights areas at high risk for oral neoplasia based on loss of collagen autofluorescence and alterations in epithelial cell NAD(P)H and FAD.
2. Develop a low-cost high resolution probe that can image epithelial cell nuclei, inflammatory cell infiltrate, and subsurface angiogenesis in oral mucosa in vivo with high resolution and high image contrast.
3. Develop a multimodal Active Biopsy Guidance imaging system by integrating the optical mapping scope and the high resolution probe into a single, compact system. The optical mapping scope will highlight areas at risk for neoplasia, automatically projecting a risk map onto the tissue; the high resolution probe will enable high-resolution imaging within high-risk areas to precisely determine when and where to biopsy tissue at risk for neoplasia based on the next generation hallmarks of cancer.

	4. Validate the ability of the fully developed Active Biopsy Guidance imaging system to provide real-time precise guidance for selection of oral biopsy sites based on severity score maps developed using the next-generation hallmarks of cancer in high-risk patients undergoing surveillance for oral cancer.
Role:	Biostatistician
Overlap:	None

(NEW)

Emerson Award	*Enhancing EGFR-Targeted Therapy by Blocking Immunosuppression in the Tumor Microenvironment in Inflammatory Breast Cancer (Wang)*
Time Commitments:	0.36 calendar months (3% effort)
Supporting Agency:	Emerson Collective
Grants Officer:	Not available for this submission
Performance Period:	03/02/2020-03/01/2022
Level of Funding:	
Goal(s):	To identify critical molecules and related mechanisms that contribute to panitumumab-induced immune response in IBC. (Effort effective 12/1/2020)
Specific Aims:	1. Identify chemokines that are regulated by the EGFR pathway and contribute to IBC aggressiveness. 2. Determine the role of chemokines in the EGFR-modulated immune response in a humanized IBC mouse model.
Role:	Collaborator
Overlap:	None

(NEW)

APOLLO Moon Shot	*Quantitative Imaging Biomarkers of Immune Response in Melanoma Brain Metastases*
Time Commitments:	1.20 calendar months (10% effort)
Supporting Agency:	MD Anderson – APOLLO Moon Shot Platform
Grants Officer:	Laura Landry, 713-745-0541, lcalvarez@mdanderson.org,
Performance Period:	09/01/2020- 08/31/2022
Level of Funding:	
Goal(s):	To develop and validate quantitative imaging biomarkers of immunophenotype and immune response in melanoma patients with brain metastases treated with immunotherapy +/- radiotherapy based on conventional and advanced magnetic resonance imaging (MRI). FUND121581
Specific Aims:	1. To quantify immune response in melanoma brain metastases undergoing stereotactic radiosurgery (SRS) and/or immunotherapy/targeted therapy via mathematical modeling of imaging-based volumetric measurement and lab data, and correlate the model prediction with clinical response. 2. To extract radiomic features from conventional T1 and T2-weighted MRI of melanoma brain metastases in patients undergoing SRS and/or immunotherapy/targeted therapy, to correlate radiomic features with immunophenotype and immune response.

3. To investigate multiparametric MRI features from diffusion weighted imaging (DWI) and perfusion weighted imaging (PWI) of melanoma brain metastases in patients undergoing SRS and/or immunotherapy/targeted therapy, to correlate parametric maps and radiomics features with immunophenotype and immune response.

Overlap: None

(THIS GRANT)
PC190353 *Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC) (Aparicio)*
Time Commitments: 0.60 calendar months (5% effort)
Supporting Agency: Department of Defense (DOD)
Grants Officer: Kenneth E. Grenier, (301) 619-2728, kenneth.e.grenier2.civ@mail.mil
Performance Period: 09/01/2020-08/31/2024
Level of Funding:
Goal(s): The overall goal is to arrive at biologically-based rational combinations to treat the AVPC with curative intent.
Specific Aims: 1. Determine the effect of durvalumab on the clinical efficacy of cabazitaxel-carboplatin induction and olaparib maintenance in men with AVPC.
2. Determine the effects of durvalumab on the immune components of the tumor microenvironment when added to cabazitaxel-carboplatin induction and to olaparib maintenance in men with AVPC.
Role: Statistician

(NEW)
N/A *Development of Novel Therapy by Targeting Tumor Microenvironment in Inflammatory Breast Cancer*
Time Commitments: 0.60 calendar months (5% effort)
Supporting Agency: Breast Cancer Research Foundation
Grants Officer: Sarah Boll
Performance Period: 10/01/2020-09/30/2021
Level of Funding:
Goal(s): To establish a novel technology for liquid biomarker discovery and to determine the role of mast cells in the EGFR-modulated immunosuppressive TME in IBC.
Specific Aims: 1. Establish liquid biomarker identification using TGIRT-seq for patients with IBC.
2. Determine the role of mast cells in modulating the EGFR-induced immunosuppressive TME and IBC tumor growth.
Overlap: None

(NEW)
R01 CA252729-01A1 *Mechanisms Associated with Organotropic Metastasis (Kalluri)*
Time Commitments: 0.60 calendar months (5% effort)
Supporting Agency: NIH/NCI
Grants Officer: Christopher L. Hatch, 240-276-6454, ch29v@nih.gov
Performance Period: 07/01/2021-06/30/2026
Level of Funding:

Goal(s):	The central hypothesis of this proposal is that vascular heterogeneity functionally contributes to organotropic metastasis.
Specific Aims:	1. Determine the impact of organ fibrosis on the tropism of breast cancer metastasis. 2. Investigate the mechanism of Ang-2 mediated organ specific vascular disruption to facilitate tropic metastasis. 3. Examine the functional contribution of claudin-5 in lung metastasis.
Role:	Co-Investigator
Overlap:	None

PREVIOUS (Recently completed)

5 U01 CA200468-05	*A Clinical Validation Center for Early Detection of Pancreatic Cancer (Maitra)*
Time Commitments:	1.468 Cal Months (12.24% effort)
Supporting Agency:	NIH/NCI
Grants Officer:	Jo Ann S Rinaudo, 240-276-7133, rinaudoj@mail.nih.gov
Performance Period:	05/04/2016-03/31/2021
Level of Funding:	
Goal(s):	To determine whether a marker combination can be developed with improved performance compared to CA19-9 for detecting early-stage PDAC.
Specific Aims:	1. To establish a multi-institutional collaborative for prospective collection of biospecimens from patients with resectable PDAC, pancreatic cysts, other benign pancreatic pathologies, and matched controls in order to facilitate biomarker validation studies. 2. To validate an antigen and autoantibody panel for early detection of PDAC in diagnostic, high-risk, and pre-diagnostic cohorts using a hybrid array platform.
Role:	Statistician
Overlap:	None

RP160693	*Acute Myeloid Leukemia in the Immunosuppressed (Andreef)*
Time Commitments:	1.20 calendar months (10% effort)
Supporting Agency:	Cancer Prevention & Research Institute of Texas (CPRIT)
Grants Officer:	Jim Willson, 512-305-8490 and 240-276-7133, jwillson@cprit.texas.gov
Performance Period:	08/31/2016-08/30/2021
Level of Funding:	
Goal(s):	To provide centralized biostatistics, bioinformatics, and database support for all Projects and Cores. (Effort ended effective 10/1/2020)
Specific Aims:	1. investigates whether oxidative phosphorylation (OXPHOS) will cause hypoxia and HIF-1 stabilization in AML cells and reprogramming of leukemia bone marrow microenvironment (BME) 2. of Project 1: In this aim, we will visualize oxygen tension and leukemia cell mobility in vivo using intravital microscopy.
Role:	Biostatistician
Overlap:	None

N/A	*Chemoprevention of Hepatocellular Carcinoma by Disrupting Crosstalk Between c-Myc-expressing Hepatocytes and Hepatic Stellate Cells (Li)*
Time Commitments:	0.12 calendar months (1% effort)

Supporting Agency:	Duncan Family Institute for Cancer Prevention and Risk Assessment Seed-funding Research Program
Grants Officer:	Mickey Lubin, 713-563-2053, mdlubin@mdanderson.org
Performance Period:	04/01/2019-03/31/2021
Level of Funding:	
Goal(s):	To develop a clinically translatable approach in chemoprevention of HCC. (Effort only, no salary support)
Specific Aims:	1. To test the hypothesis that low dose M-CPA/PTX will reduce the incidence and tumor burden in a c-Myc-driven transgenic mouse model of HCC. 2. To test the hypothesis that low dose M-CPA/PTX will reduce liver inflammation and fibrosis through disruption of crosstalk between hepatocytes and HSCs.
Role:	Collaborator
Overlap:	None

ARP-18-006	*Development of Novel Combinational Therapy with Enzalutamide in AR+ TNBC (Ueno)*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	Breast Cancer Research Foundation
Grants Officer:	Sarah Boll, MSWL, 646-497-2628, sboll@bcrf.org,
Performance Period:	06/30/2019-06/30/2021
Level of Funding:	
Goal(s):	Our central hypothesis, which is based on our preliminary findings, is that specific suppression of kinase activity in AR+ TNBC enhances enzalutamides anti-tumor activity.
Specific Aims:	1. Identify kinase-targeted inhibitors that increase the efficacy of nzalutamide in AR+ TNBC. 2. Identify candidate biomarkers predictive of response to enzalutamide plus kinase-targeted inhibitor in AR+ TNBC.
Role:	Co-Investigator
Overlap:	None

SHETH, Rahul

CURRENT

P30 CA016672	*Systemic Tumor Immunity by Intratumoral Drug Delivery and Radiation Therapy (Pisters)*
Effort:	0 calendar months
Supporting Agency:	MD Anderson-CCSG Radiation Oncology/Cancer Imaging Pilot Grant
Grants Officer:	Leslie Hickman, Grants Mgt Specialist, 301-631-3009, hickmanl@mail.nih.gov
Performance Period:	10/01/2018-09/30/2021
Level of Funding:	
Goal(s):	Characterize the local and abscopal effects of XRT when combined with intratumoral immunotherapy.
Specific Aims:	1. Characterize the local and abscopal effects of XRT when combined with intratumoral immunotherapy.
Overlap:	None

R21 EB026089 — *Molecularly Targeted Photothermal Ablation to Enhance the Therapeutic Efficacy of Immunomodulatory Therapies in Hepatocellular Carcinoma (Sheth)*

Effort: 1.20 calendar months (10% effort)
Supporting Agency: NIH/NIBIB
Grants Officer: Katie Ellis, 301-451-4791, katie.ellis@nih.gov
Performance Period: 01/19/2019-11/30/2021
Level of Funding:
Goal(s): Define the adaptive immune response following tumor-specific hyperthermic stress, and to determine changes in soluble oncogenic factors following tumor specific hyperthermia versus RFA.
Specific Aims: 1. Define the adaptive immune response following tumor-specific hyperthermic stress.
2. Determine changes in soluble oncogenic factors following tumor-specific hyperthermia versus RFA
Overlap: None

(NEW)
N/A — *Cryoablation Combined with Stereotactic Body Radiation Therapy for the Treatment of Painful Bone Metastases (Sheth)*

Time Commitments: 1.20 calendar months (10% effort)
Supporting Agency: BTG Strategic Alliance
Grants Officer: Yaa Adjei
Performance Period: 10/01/2020-12/31/2022
Level of Funding:
Goal(s): To determine the efficacy of cryoablation in combination with stereotactic body radiation therapy (SBRT) or SBRT only for the treatment of painful bone metastases.
Specific Aim: 1. To investigate the local microenvironmental changes following SBRT and cryoablation combined with SBRT to bone metastases.
Overlap: None

(NEW)
N/A — *Collaborative Research: CPS: Medium: A CPS Approach To Tumor Immunomodulation; Sensing, Analysis, And Control To Prime Tumors to Immunotherapy*

Effort: 0.12 calendar months (1% effort)
Supporting Agency: National Science Foundation (NSF)
Grants Officer: Irene C. Sattler, isattler@nsf.gov
Performance Period: 07/15/2021-06/30/2024
Level of Funding:
Goal(s): The CPS program aims to develop the core research needed to engineer these complex CPS, some of which may also require dependable, high confidence, or provable behaviors.
Specific Aims: 1. In vivo measurements and immune profiling will be conducted in male and female mice (n=20), randomly allocated in a 1 :1 ratio to experimental groups at age 2 months.

2. In this experiment, we will determine the influence of therapies targeting tumor microenvironmental biophysical properties both discretely and in concert with immunotherapies.

Overlap: None

(THIS AWARD)

PC190353 *Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC) (Aparicio)*

Time Commitments: 0.60 calendar months (5% effort)
Supporting Agency: DOD
Grants Officer: Kenneth E. Grenier, 301-619-2728, kenneth.e.grenier2.civ@mail.mil
Performance Period: 09/01/2020-08/31/2024
Level of Funding:
Goal(s): The overall goal of this study is to arrive at biologically-based rational combinations to treat the AVPC with curative intent.
Specific Aims: 1. Determine the effect of durvalumab on the clinical efficacy of cabazitaxel-carboplatin induction and olaparib maintenance in men with AVPC.
2. Determine the effects of durvalumab on the immune components of the tumor microenvironment when added to cabazitaxel-carboplatin induction and to olaparib maintenance in men with AVPC.

PREVIOUS (Recently completed)

IRG *A Controlled Released Injectable Biomaterial for Intratumoral Immunotherapy*

Effort: 0 calendar
Supporting Agency: MD Anderson Institutional Review Grant
Grants Officer: Carrie Feighl, Director, Research Finance, 713-792-3477, research_finance@mdanderson.org
Performance Period: 01/01/2020-01/01/2021
Level of Funding:
Goal(s): The overall objectives of this proposal are to overcome barriers to i.t. immunotherapy imposed by poor drug release kinetics and an unreceptive tumor microenvironment.
Specific Aims: 1. Mechanistically characterize the pharmacologic and immunologic advantages of STING-hydrogel i.t. delivery.
2. Evaluate the biomechanical and immunologic ramifications of i.t. hyaluronidase.
Overlap: None

SIR2018 *Antitumor Adaptive Immune Activation by Molecularly Targeted Photothermal Ablation for the Treatment of Hepatocellular Carcinoma (Sheth)*

Effort: 0.12 calendar months (1% effort)
Supporting Agency: Society for Interventional Radiology
Grants Officer: Audrey Ford, Sir Foundation, 703-460-5580, aford@sirweb.org
Performance Period: 07/01/2018- 06/30/2021
Level of Funding:
Goal(s): We propose a minimally invasive, tumor-specific thermal ablation modality to overcome key barriers to adaptive antitumor immune

activation for hepatocellular carcinoma (HCC). We believe that this modality will offer higher precision tumor treatments with decreased off-target oncogenic effects and increased tumoricidal immune activation compared to conventional ablation.

Specific Aims: 1. Define the adaptive immune response following tumor-specific hyperthermic stress.
2. Determine changes in cytokine profiles following tumor-specific hyperthermia versus conventional ablation.

Overlap: None

SUBUDHI, Sumit

CURRENT

NCT03177460 *2017-0103: A Pilot Presurgical Study of Daratumumab (CD38 Antagonist) or JNJ-40346527 in Men with High-Risk Localized Prostate Cancer Followed by Radical Prostatectomy (Subudhi)*

Time Commitments: 0.12 calendar months (1% effort)
Supporting Agency: Janssen Pharmaceuticals Inc.
Grants Officer: Chantal Lanoue, CLanoue@its.jnj.com
Performance Period: 01/18/2017-01/17/2022
Level of Funding:
Project Goals: To learn about the safety and tolerability of giving Darzalex (daratumumab) or JNJ-527 (JNJ-40346527) to patients who have prostate cancer before having an already-scheduled prostatectomy.
Specific Aims: Not applicable.
Overlap: None

2016-0848 *A Phase 2 trial of Nivolumab plus Ipilimumab (Subudhi)*

Time Commitments: 0 calendar months
Supporting Agency: BMS Immune Alliance
Grants Officer: Laurie Kopacz, laurie.kopacz@bms.com
Performance Period: 01/23/2017-01/22/2022
Level of Funding:
Goal(s): The purpose of this study is to determine whether nivolumab plus ipilimumab has preliminary evidence of safety and effectiveness in the treatment of participants with metastatic castration-resistant prostate cancer who have progressed after prior docetaxel-containing regimen.
Specific Aims: Not applicable.
Overlap: None

D2018-014 *Targeting the Immunosuppressive Compartment of the Prostate Cancer Bone Metastatic Microenvironment to Improve Clinical Outcomes (Subudhi)*

Time Commitments: 9.0 calendar months (75% effort)
Supporting Agency: V Foundation/Lloyd Fam Clin Oncol Scholar Award
Grants Officer: Sommer Axner, 919-443-3553, saxner@v.org
Performance Period: 02/01/2018-02/01/2022 NCE
Level of Funding:
Project Goals: To improve clinical outcomes in patients with advanced prostate cancer through rationally designed immune checkpoint therapy-based

	combinatorial strategies that target the immunosuppressive tumor microenvironment.
Specific Aims:	1. To improve clinical outcomes by overcoming adaptive resistance within the tumor microenvironment. 2. To improve effector immune responses within the tumor microenvironment. 3. Conduct co-clinical trials in murine models to identify novel T cell and macrophage targets.
Overlap:	None

NCT03204812	*2016-0769:A Pilot Trial to Explore the Link Between Immunological Changes and Efficacy of Tremelimumab plus Durvalumab (MEDI4736) in Chemotherapy-naive Men with Metastatic Castration-Resistant Prostate Cancer (CRPC) (Subudhi)*
Time Commitments:	0.12 calendar months (1% effort)
Supporting Agency:	AstraZeneca
Grants Officer:	Ferdinand Udoye, ferdinand.udoye@astrazeneca.com
Performance Period:	05/12/2017-05/11/2022
Level of Funding:	
Goal(s):	This phase II trial studies the safety, tolerability and how well durvalumab and tremelimumab work in treating participants with castration-resistant prostate cancer who have not received chemotherapy (chemotherapy naïve) and has spread to other places in the body (metastatic). Immunotherapy with monoclonal antibodies, such as durvalumab and tremelimumab, may help the body's immune system attack the cancer, and may interfere with the ability of tumor cells to grow and spread.
Specific Aims:	1. To evaluate the safety and tolerability of durvalumab plus tremelimumab in patients with metastatic castration-resistant prostate cancer. 2. To assess the efficacy of durvalumab plus tremelimumab in patients with metastatic castration-resistant prostate cancer. 3. To explore immunological changes in peripheral blood and tissue (e.g. peripheral blood cluster of differentiation [CD] 4+ [Inducible COStimulator (ICOS)]+ T cells, CD3 expression in tissue) in response to durvalumab plus tremelimumab in patients with metastatic castration-resistant prostate cancer.
Overlap:	None

(Received a no-cost extension)

P50 CA140388-10	*MD Anderson Cancer Center Prostate Cancer SPORE (Logothetis/Thompson)* *Project 1: Integrating Ipilimumab Immunotherapy with Approved Treatment Strategies in CRPC*
Time Commitments:	0.60 calendar months (5% effort)
Supporting Agency:	NIH/NCI
Grants Officer:	Ashley Salo, ashley.salo@nih.gov
Performance Period:	09/01/2016-08/31/2022 NCE
Level of Funding:	

Goal(s):	To rationally integrate anti-CTLA-4 (ipilimumab) immunotherapy with agents targeting the AR signaling pathway to provide durable clinical benefit with improved survival in patients with prostate cancer and utilize novel imaging techniques to accurately identify tumor responses.
Specific Aims:	1. Identify biological changes indicative of mechanistic pathways that contribute to clinical outcomes in matched tumor and blood specimens obtained from prostate cancer patients given drugs targeting the AR signaling pathway plus anti-CTLA-4 (ipilimumab) immunotherapy. 2. Determine clinical outcomes after treatment with AR-targeting agents (ARN-509 + abiraterone acetate) followed by concurrent anti-CTLA-4 (ipilimumab) immunotherapy and prospectively evaluate the effectiveness of selected biological pathways identified in Aim 1 to be indicative of mechanistic pathways that contribute to clinical outcomes. 3. Determine the efficacy of targeting B7-H3 and B7-H4 with radiolabeled monoclonal antibodies as a non-invasive means to detect prostate cancer.
Role:	Co-Investigator
Overlap:	None

(NEW)

Prostate Moon Shot	*Prostate Cancer Moon Shot* *Project 3: Development of Rational Immunotherapy Combinations to Overcome the Immunosuppressive Prostate Tumor Microenvironment* (Logothetis/Aparicio/Navin)
Time Commitments:	0 calendar months
Supporting Agency:	MD Anderson Moon Shot Program
Grants Officer:	Carrie C. Feighl, 713-792-3477, Research_Finance@mdanderson.org
Performance Period:	09/01/2021-08/31/2022
Level of Funding:	
Project Goals:	To improve clinical outcomes in patients with advanced prostate cancer through rationally designed ICT-based combinatorial strategies that target the immune-suppressive tumor microenvironment.
Specific Aims:	1. To identify novel correlative markers for responsiveness to combined immune checkpoint blockade (anti-CTLA-4 plus anti-PD-[L]1). 2. To therapeutically modulate immunosuppressive myeloid cells with a CSF1R antagonist.
Role:	Co-Leader
Overlap:	None

NCT03551782	*2017-0811: An Open-label, Multicenter, Phase 1b Study of JNJ-63723283, a PD-1 Inhibitor, Administered in Combination with Apalutamide in Subjects with Metastatic Castration- Resistant Prostate Cancer (Subudhi)*
Time Commitments:	0 calendar months
Supporting Agency:	Janssen Pharmaceuticals Inc.
Grants Officer:	Kimberly Bernard, KBernar4@ITS.JNJ.com
Performance Period:	08/14/2018-12/18/2022
Level of Funding:	
Goal(s):	The purpose of this study is to evaluate the safety of the combination of cetrelimab, with apalutamide and to define a population of participants

	with metastatic castration-resistant prostate cancer (mCRPC) who respond to treatment with the combination of cetrelimab and apalutamide.
Specific Aims:	Not applicable.
Overlap:	None
NCT03431350	*2017-0952: A Phase 1b-2 Niraparib Combination Therapies for the Treatment of Metastatic Castration-Resistant Prostate Cancer (Subudhi)*
Time Commitments:	0 calendar months
Supporting Agency:	Janssen Research and Development LLC
Grants Officer:	Kerri Anne Sitze, KSitze@ITS.JNJ.com
Performance Period:	02/27/2018-04/14/2023
Level of Funding:	
Goal(s):	The purpose of this study is to: a) establish the recommended phase 2 dose (RP2D) and to evaluate the antitumor activity and safety of niraparib combination therapies (Combinations 1 and 2) and b) to determine the relative bioavailability of niraparib and abiraterone acetate (AA) in combination (Combination 3) in participants with metastatic castration-resistant prostate cancer (mCRPC).
Specific Aims:	Not applicable
Overlap:	None
(NEW)	
N/A	*RFA IO Combinations (Giancotti)*
Time Commitments:	0 calendar months
Supporting Agency:	Janssen Research & Development, LLC
Grants Officer:	Jhilik De, Administrative Contact, 215-793-7348, jde5@its.jnj.com and Brent Rupnow: brupnow@ITS.JNJ.com
Performance Period:	08/01/2019-07/31/2024
Level of Funding:	
Goal(s):	To evaluate the effects of standard of care alone, or in combination with immuno-oncology (IO) drugs, in controlling myeloid and T cell populations in prostate cancer.
Specific Aims:	Not applicable.
Role:	Co-Investigator
Overlap:	None
(THIS AWARD)	
W81XWH-20-1-0257	*PC190353: Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC) (Aparicio)*
Time Commitments:	1 calendar months (1% effort)
Supporting Agency:	Department of Defense
Grants Officer:	Kenneth E. Grenier, 301-619-2728, kenneth.e.grenier2.civ@mail.mil
Performance Period:	09/01/2020-08/31/2024
Level of Funding:	
Goal(s):	Our overall goal is to arrive at biologically-based rational combinations to treat the AVPC with curative intent.
Specific Aims:	1. Determine the effect of durvalumab on the clinical efficacy of cabazitaxel-carboplatin induction and olaparib maintenance in men with AVPC.

	2. Determine the effects of durvalumab on the immune components of the tumor microenvironment when added to cabazitaxel-carboplatin induction and to olaparib maintenance in men with AVPC.
Role:	Co-Investigator
Overlap:	None

(NEW)

NCT03835533	*2019-0140: A Multicenter, Open-Label, Exploratory Platform Study to Evaluate Biomarkers and Immunotherapy Combinations for the Treatment of Patients with Metastatic Castration Resistant Prostate Cancer (Subudhi)*
Time Commitments:	0 calendar months
Supporting Agency:	Parker Institute for Cancer
Grants Officer:	Ari Bitton, abitton@parkerici.org
Performance Period:	11/14/2019-11/13/2026
Level of Funding:	
Goal(s):	This study is designed to evaluate multiple clinical hypotheses and mechanistically-defined combinations to evaluate the safety and efficacy of immunotherapy combinations in participants with mCRPC who have received prior secondary androgen receptor signaling inhibitor therapy (eg, abiraterone, enzalutamide, apalutamide).
Specific Aims:	Not applicable.
Overlap:	None

(NEW)

NCT04052204	*2019-0508: A Phase 1b/2 Study to Evaluate Safety and Clinical Activity of Avelumab in Combination with Bempegaldesleukin (NKTR-214) with or without Talazoparib or Enzalutamide in Participants with Locally Advanced or Metastatic Solid Tumors (Subudhi)*
Time Commitments:	0 calendar months
Supporting Agency:	Pfizer Inc.
Grants Officer:	KarenMaksin, Karen.Maksin@pfizer.com
Performance Period:	11/21/2019-11/20/2026
Level of Funding:	
Goal(s):	Evaluation of the combination of avelumab + bempegaldesleukin (NKTR-214) in locally advanced squamous cell carcinoma of the head and neck (metastatic SCCHN) and avelumab + bempegaldesleukin (NKTR-214) + talazoparib or enzalutamide in metastatic castration resistant prostate cancer (mCRPC).
Specific Aims:	Not applicable
Overlap:	None

(NEW)

NCT04100018	*2020-0072: Advance Funding-Rapid Activation Program-2020-0072-A Phase 3 Randomized, Double-Blind Study of Nivolumab or Placebo in Combination with Docetaxel, in Men with Metastatic Castration-resistant Prostate Cancer, protocol number CA209-7DX (Subudhi)*
Time Commitments:	0 calendar months
Supporting Agency:	Bristol-Myers Squibb
Grants Officer:	Michelle Kirchoff, michelle.kirchoff@syneoshealth.com

Performance Period: 05/04/2020-05/03/2027
Level of Funding:
Goal(s): The purpose of this study is to test the safety and effectiveness of nivolumab with docetaxel in men with advanced castration resistant prostate cancer who have progressed after second-generation hormonal manipulation.
Specific Aims: Not applicable
Overlap: None

(NEW)
NCT04381832 *2020-0376: A Phase 1b/2, Open-Label, Randomized Platform Study Evaluating the Efficacy and Safety of AB928-Based Treatment Combinations in Patients with Metastatic Prostate Cancer (Subudhi)*
Effort: 0 calendar months
Supporting Agency: Arcus Biosciences
Grants Officer: Amy Ford, Amy.Ford@iqvia.com
Performance Period: 06/24/2020-06/23/2027
Level of Funding:
Goal(s): This is a Phase 1b/2, open-label, multicenter platform trial to evaluate the antitumor activity and safety of etrumadenant (AB928)-based combination therapy in participants with metastatic castrate resistant prostate cancer (mCRPC).
Specific Aims: Not applicable.
Overlap: None

(NEW)
NCT04631601 *2020-0568: A Master Protocol Evaluating the Safety and Efficacy of Therapies for Metastatic Castration-resistant Prostate Cancer (mCRPC) (Subudhi)*
Time Commitments: 0 calendar months
Supporting Agency: Amgen Inc.
Grants Officer: Amanda Pratt, amandap@amgen.com
Performance Period: 11/04/2020-11/03/2027
Level of Funding:
Goal(s): This is a master protocol designed to evaluate the safety and efficacy of investigational therapies in participants with metastatic castration-resistant prostate cancer (mCRPC).
Specific Aims: Not applicable
Overlap: None

PREVIOUS (Recently completed)
NCT03792841 *2018-1122: Amgen Start-Up Cost Payment Letter*
A Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Prostate Specific Membrane Antigen Half-life Extended Bispecific T-cell Engager AMG 160 in Subjects with Metastatic Castration-resistant Prostate Cancer (Subudhi)
Time Commitments: 0 calendar months
Supporting Agency: Amgen Inc.
Grants Officer: Amanda Pratt, amandap@amgen.com
Performance Period: 07/16/2020-07/16/2021

Level of Funding:
Project Goals: A study to evaluate the safety and tolerability of AMG 160 and in combination with pembrolizumab in adult subjects with metastatic castration-resistant prostate cancer (mCRPC) and determine the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D).
Specific Aims: Not applicable.
Overlap: None

ZHANG, Miao

CURRENT

(NEW)

W81XWH-21-1-0522 *PC200420: Targeting Histone Lysine Demethylase KDM4A in Neuroendocrine Prostate Cancer (Wang)*
Time Commitments: 0.36 calendar (3% effort), Year 3 only
Supporting Agency: DOD-PCRP-Idea
Grants Officer: Kimberly Carter, 301-619-2249, Kimberly.m.carter47.civ@mail.mil
Performance Period: 09/01/2021-08/31/2024
Level of Funding:
Goal(s): Our overall goal is to develop combination therapy to improve the clinical outcome of platinum-taxane chemotherapy in patients with NEPC.
Specific Aims: 1. Determine the role of KDM4A in NEPC progression using organoids, PDXs, and GEMMs.
2. Examine the mechanism(s) by which KDM4A regulates UPR signaling.
3. Determine whether KDM4 inhibitors improve the therapeutic outcomes of platinum-taxane chemotherapy in NEPC.
Role: Co-Investigator
Overlap: None

(THIS AWARD)

PC190353 *Chemoimmunotherapy for Aggressive Variant Prostate Cancers (AVPC) (Aparicio)*
Time Commitments: 0.12 calendar months (1% effort), Year 1; 0.60 calendar months (5% effort), Year 2; 1.20 calendar months (10% effort), Years 3 and 4
Supporting Agency: DOD
Grants Officer Kenneth E. Grenier, 301-619-2728, kenneth.e.grenier2.civ@mail.mil
Performance Period: 09/01/2020-08/31/2024
Level of Funding: total
Goal(s): The overall goal is to arrive at biologically-based rational combinations to treat the AVPC with curative intent.
Specific Aims: 1. Determine the effect of durvalumab on the clinical efficacy of cabazitaxel-carboplatin induction and olaparib maintenance in men with AVPC.
2. Determine the effects of durvalumab on the immune components of the tumor microenvironment when added to cabazitaxel-carboplatin induction and to olaparib maintenance in men with AVPC.
Role: Co-Investigator

PREVIOUS (Recently completed)

None.

What other organizations were involved as partners?

Organization Name:	Janssen Pharmaceuticals.
Location of Organization:	Headquarters in Beerse, Belgium.
Partner's contribution to the project:	Provides cetrelimab and niraparib.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

Nothing to report.

QUAD CHARTS:

Not applicable.

9. APPENDICES:

Not applicable