AD_____

Award Number: W81XWH-09-1-0144

TITLE: University of Washington Prostate Cancer Clinical Trials Consortium Application

PRINCIPAL INVESTIGATOR: Celestia Higano

CONTRACTING ORGANIZATION: University of Washington
Seattle, WA 96195

REPORT DATE: April 2011

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
01-04-2011	Annual	1 APR 2010 - 31 MAR 2011

4. TITLE AND SUBTITLE
University of Washington Prostate Cancer Clinical Trials Consortium Application

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-09-1-0144

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Celestia Higano

E-Mail: thigano@uw.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Washington
Seattle, WA 96195

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Purpose. Maintain active and productive status as a member of the Prostate Cancer Clinical Trials Consortium throughout the funding period. Scope. Since the annual report of April 2010, the University of Washington continues to be an active contributing member of the PCCTC, fulfilling goals set forth in the Statement of Work. Major progress. This last year, we opened 3 trials, and introduced 3 LOIs to the Consortium. We are opening 5 additional therapeutic trials and have agreed to participate in 2 additional trials. We enrolled 42 patients on therapeutic trials and 7 patients on Consortium biomarker validation (phase III) trials. We are authors on 9 Consortium abstracts2 manuscripts, (all abstracts presented or to be presented at ASCO, AUA, and GU ASCO). An active plan to recruit minority/disproportionately affected populations is a high priority and therefore in constant evolution. Our recruitment in this area matches the regional proportion of these populations. Results. We continue to develop and grow our infrastructure that supports active, productive Consortium participation and which has enabled us to reach the stated goals for patient accrual and LOI proposals. Significance. The Consortium provides a mechanism for participation in early clinical development of novel agents and rapid testing of these agents for the treatment of prostate cancer. At our institution, our scientific/ SPORE/PCF Challenge grant and Consortium clinical research goals are complimentary. Validation of biomarkers is of great significance for shortening the time to drug approval and availability of new agents to patients with prostate cancer.

15. SUBJECT TERMS
prostate cancer, phase I/II, phase II, randomized phase II, clinical consortium

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	36	**19b. TELEPHONE NUMBER** *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

Page

KEY ACCOMPLISHMENTS
University of Washington

Our key accomplishments from 4/1/10-3/31/11 are listed below.

Infrastructure:

Central Infrastructure:

- Attended all PCCTC face to face meetings including the following: June 3-4, 2010 before ASCO meeting in Chicago, September 22-23, 2010 meeting prior to Prostate Cancer Foundation Scientific Retreat, November 17-18, 2010 DOD Annual Review, Falls Church, VA, and February 16, 2011 prior to GU ASCO meeting, Orlando, FLA.

- Attended IMPaCT Meeting, March 9-11, 2011, Orlando, FLA. Dr. Higano made presentations at the Plenary Session on behalf of PCCTC regarding immunotherapy trials and at a "Meet the Expert" session on "Understanding and monitoring the toxicities of androgen deprivation".

- Actively participated in the monthly Consortium PI and bi-weekly Coordinator teleconferences.

- Participated in central budgeting and contracting; provided input to Coordinating Center regarding missing budget items to be considered in contract development.

- Provided leadership as Co-chair of the Consortium Publications Committee and Correlative Science Committee.

- Contributed to trial design of Consortium trials led by other sites

- Attended and participated in Annual Prostate Cancer Foundation Scientific Retreat 2010

Local Infrastructure:

- Held twice monthly protocol development, review, and prioritization meetings with investigators at UWash and UBC, one dedicated to local disease and one to advanced disease trials.

- Established additional satellite sites through the SCCA Network Partner Sites.

- Actively working on incorporating new HMO SCCA Network site (Group health Cooperative) as a source of clinical trial candidates.

- Actively engaged in minority/disproportionately affected population outreach and increased outreach activities through SPORE Advocacy group, local support groups, state legislative committees, American Cancer Society, Fred Hutchinson Cancer Research Center Minority Outreach Coordinator.

- Physicians and staff volunteered at and attended numerous local prostate cancer awareness events in an effort to educate people about the importance of early detection and the need to participate in clinical trials to make progress.

- Transitioned from manual to automated request and entry of CAISIS research data repository consent system. The clinical research team uses data in Caisis to complete case report forms, to screen for trial eligible patients, and as a tool for data collection on investigator initiated Consortium trials.

- Hosted the 10th Annual Pacific NW Prostate Cancer Conference with OHSU attended by over 200 men and their family members.

Research / Protocol Development

- Opened 3 therapeutic Consortium trials.

- 5 additional therapeutic Consortium trials initiated and pending activation at UWash.

- Agreed to participate in 2 additional trials. Awaiting final protocol documents to initiate trial start-up procedures.

- Directly participated in the protocol development of 3 Consortium trials this year.

- Collected over 531 correlative biological samples.

- Presented 3 LOIs for Consortium consideration: 1 accepted and 2 rejected. The two rejected trials will be re-presented as biomarker trials.

- During funding period, 4/1/10-3/31/11, UWash has enrolled 42 patients on therapeutic trials and 7 on biomarker studies. This year's accruals were impaired by either unexpected closure of several trials preceded by long periods on "hold" and the large percentage of trials in phase I (5/13 or 38%) that are expected to have only intermittent accrual due to the need to observe cohorts over time.

ANNUAL REPORT — DETAILED REPORT BODY
University of Washington

As a consortium research site, UWash fulfilled the following tasks listed in our original SOW.

Task 1. Attend Pre-Award Meeting

There was no pre-award meeting during the reporting period. Drs. Higano, Yu and UWash Consortium team members attended the pre-award meetings in November 2006 and in 2008.

Task 2. Organize Clinical Research Site Consortium Infrastructure

Maintain operational procedures with UBC

The UWash continues to collaborate with UBC and discuss scientific priorities and protocol details. The investigators at UBC are included in monthly local PCCTC Working Group Meetings. Dr. Kim Chi (UBC) is the overall study Principal Investigator (PI) 2 trials (07-008 and 11-026) and has enrolled 6 patients over this funding period; UBC will also contribute to 09-030.

Data entry

CAISIS: The UWash informatics team continues to upgrade and enhance our local Caisis data repository in anticipation of implementing centralized data management for investigator initiated Consortium trials. UWash had agreed to pilot the first study to be tested in the new web-based CAISIS data entry system for the upcoming 09-028. We will also use Caisis for data collection for the upcoming 10-070 trial lead by Duke.

Central budget and contract processes

UWash continues to contribute to building a successful central budgeting effort and has provided costing information and suggestions to the template budget format developed by the Consortium Coordinating Center.

Contractual agreement for Site participation in the Consortium

Completed during previous funding year.

Expanding institutional accrual opportunities

In an effort to expand institutional accrual opportunities, UWash is working with the Seattle Cancer Care Alliance (SCCA) Network Affiliate partners in the community. These and selected local practices receive quarterly correspondence that reviews our open clinical trials Investigators often attend local support groups to discuss new agents and on-going trials. Recently, a large HMO in Washington and northern Idaho covering over 674,900 residents, joined the SCCA Network. It is hope that this addition to the Network will further enhance our accrual in the coming years. At our monthly SPORE Advocates Committee meeting, there is always at least one presentation of active clinical trials. Each year, in conjunction with OHSU, we host a meeting held in both Seattle and Portland for prostate cancer patients and families during which we discuss the value of clinical research and present our on-going trials. See Task 7, #6 for further efforts to expand institutional accrual opportunities. (See Tables A and B in supporting documentation.)

Correlative and biomarker studies

During the last funding period, UWash has collected correlative samples on 7 Consortium studies, including pharmacokinetic, circulating tumor cells, and agent-specific antibody

samples, metabolic and immunologic markers and three phase III biomarker validation trials (531 samples over the last year).

UWash utilized the PCWG2 Bone Scan Assessment Worksheet to collect tumor progression data in 30 patients, at 88 time points, across 6 Consortium trials during this funding year. (See Tables A and B in supporting documentation.)

In January 2011, UWash participated in the biospecimen survey solicited by the Coordinating Center.

Participation in Consortium working groups

UWash Consortium members play active roles in the overall Consortium infrastructure. Dr. Higano is participating in the radium 223 working group and Dr. Yu is a member of the Imaging Group. Dr. Celestia Higano is the co-chair of the Consortium Publications Committee and Dr. Peter Nelson is the chair of the Consortium Correlative Science Committee.

Participation in the 2011 IMPaCT Meeting

Dr. Higano participated in the planning calls for two sessions at the 2011 IMPaCT Meeting. At the plenary session reviewing the accomplishments of the PCCTC, Dr. Higano discussed the immunotherapy trials within the Consortium. In a "Meet the Expert" session, she spoke on the side effects of androgen deprivation therapy. Dr. Higano also contributed an abstract summarizing the UWash clinical data for the 96 patients in the "warm autopsy" program.

Contribution to Consortium Protocol Development and Trial Design

In the one-year funding period, UWash was the lead site on the following 6 trials: 07-008 (OGX 427 Phase I), 08-005 (HE-3235), 08-015 (Dasatinib PET), 09-046 (TOK-001), 10-060 (Phase I doc MLN8237), 11-081 (OGX 427 Phase II). Two of these trials (07-008 and 08-005), both phase I trials, completed enrollment in late Fall of 2010.

Although not the lead site, UWash investigators/scientists also participated in the development and design of protocols that were on-going during the last year including 09-028 (exogenous testosterone), 09-030 (OGX-011 doc pain), 09-039 (KX2-391), and 09-056 (radium 223) studies led by other sites.

As scientific advisors and/or investigators in early phase trials, UW investigators participated in the design of the following phase III trials and participated in the biomarker validation studies: 09-002 (COU 301), 09-003 (AFFIRM), 09-004 (S0421), 09-005 (COU 302), 09-006 (doc dasatinib).

Task 3. Maintain Communications with Consortium Sites and Coordinating Center

The UWash Clinical Research Coordinators (CRC) participate in each bi-weekly CRC conference calls during which protocol accrual, trial start-up status and LOIs are reviewed. UWash CRC individually also communicate frequently with the Coordinating Center CRC Mary Warren, Jake Vinson, and Kristen Hakuta regarding Consortium logistics and operational procedures. The UWash CRC maintain regular communications with other Consortium sites for Consortium studies regarding budgeting, patient entry criteria, and toxicity monitoring purposes.

The UWash PI and/or co-PI participates in all scheduled monthly PI conference calls. The PI maintains an active email and telephone communications with the Coordinating Center for site

specific questions, concerns, or suggestions. In the last year, the Lead PIs for PCCTC trials held regular conference calls to discuss toxicity and efficacy of phase I agents [Montgomery-TOK-001(09-046) and HE-3235 (08-005), Higano-MLN8237 (10-060), Yu OGX-427 (07-008) and dasatinib PET (08-015)] and, as a participating site, Dr. Yu joined the weekly teleconferences with other participating site investigators to review toxicity of KX2-391 (09-047) study. Dr. Higano reviewed toxicity data for the Phase I radium 223 trial with the PI (Morris) and joined the working group on a conference call with the phase I investigators and sponsor to plan the future direction of the trial.

In the last year, UWash has suggested that the Coordinating Center present a "cumulative lessons learned" document that would summarize our collective experience in budgeting for trials. This issue arose in the context of dealing with hundreds of queries and realizing that this added work had not been covered in our budget process. This is now a work in progress and will hopefully provide metrics that will improve individual site negotiations with sponsors.

Task 4. Determine Participation in Consortium Trials

All Letters of Intent (LOI) submitted to and accepted by the Consortium are presented at our local site's PCCTC/research meetings. Each LOI is discussed for its scientific merit, feasibility, overlap with other trials, and funding source (see attached Protocol Evaluation Form -- appendix A). Our decision to participate in Consortium trials is based both on our own institutional research priorities outlined in the Introduction and the availability of "space" within a given disease state. This year, UWash has opened 3 PCCTC trials: 09-030 (OGX-11-10 doce pain), 09-039 (KX2-391), 10-060 (MLN-8237). Another 5 trials will be activated over the next two months: 09-047 (Neo-Provenge), 09-056 (radium 223), 10-072 (Aragon 509), 11-079 (XL-184), and 11-081 (OGX-427 phase II). We have also committed to 2 additional trials 10-070 (BKM-120) and 10-075 (MAOA) and are awaiting the final protocols in order to begin study start-up activities. See Tables C and D in supporting documentation.)

Task 5. Present at Least One Trial per Year to Consortium

Over the last year, UWash has submitted 3 LOIs to the Consortium including (See Table C in the Supporting Documents.) A capsule description of each trial is included below.

c10-068 "A Randomized Phase II Study of Combined Androgen Deprivation Versus Combined Androgen Deprivation with IMC-A12 for Patients with New Hormone Sensitive Metastatic Prostate Cancer (SWOG 0925)"

This is a SWOG trial co-chaired by Drs. Yu and Higano. This work spawns from institutional work with the IGF axis. The SCCA is the central lab for the CTC biomarkers and FHCRC is looking at novel microRNA biomarker; Steve Plymate's lab is looking at other pertinent correlatives related to his SPORE project. Since four SWOG sites, UWash, University of Michigan, Wayne State, and OHSU, are also members of the PCCTC, and since there is already a SWOG biomarker trial within the Consortium, this study was proposed as a Consortium study; it was hoped that this trial would develop direct collaboration between the PCCTC, SWOG, and SPORE mechanisms.

This LOI was not accepted as a therapeutic protocol due to its' origination in a cooperative group, despite the fact Drs. Yu, Higano, and Hussain were all involved in the protocol design and writing. As we are conducting informative biomarker studies, we will request that this study be considered for biomarker credit.

c11-081 "A Randomized Phase II Study of OGX-427 (a Second-Generation Antisense Oligonucleotide to Heat Shock Protein-27) in Patients with Castration Resistant Prostate Cancer Who Have Not Previously Received Chemotherapy for Metastatic Disease"

OGX-427 is a second generation antisense oligonucleotide (ASO) that inhibits expression of Hsp27. This Phase 2 study has been designed to evaluate the anti-tumor effects of OGX-427 plus low-dose prednisone versus low dose prednisone alone in men with CRPC who have not previously received chemotherapy for metastatic or locally recurrent disease. This study extends the Pacific Northwest SPORE based collaboration with UBC and OHSU, as well as an builds upon our phase I experience within the Consortium with this compound.

b10-008 "A Randomized Phase 3 Study Comparing Standard First-Line Docetaxel/Prednisone to Docetaxel/Prednisone in Combination with Custirsen (OGX-011) in Men with Metastatic Castrate Resistant Prostate Cancer"

The trial was not accepted as a biomarker trial. The reason for this denial was not transparent, however, an amendment to this trial is being considered and, if CTCs are added to the trial, this will be resubmitted. This Phase 3 study has been designed to confirm that adding custirsen to standard first-line

Task 6. Enroll Patients to PCCTC Protocols

Accrual to therapeutic trials over the last year includes 42 total patients, of whom 2 are from minority/disproportionately affected populations. Our accrual is affected in part by the repertoire of phase one agents [OGX-427 (07-008), TOK-001 (09-046), MLN-8237 (10-060), HE-3235 (08-005), KX2-391 (039)] in our program (5 of 13 therapeutic trials open over the last year) as well as our willingness to participate in an acknowledged "difficult to accrue to" trial that is forging a potential new pathway to drug approval based on clinical benefit 09-030 [OGX-11-10 doc pain trial (09-030)] The accrual over the last 4 months has been slower than usual, impacted by the "hold" and then closure (November 2010) of 08-015 (nilutamide or dastinib biopsy trial) that also affected the companion trial 08-019 (dasatinib PET study). This could be further exacerbated by the delay in the anticipated opening of the phase II portion of 09-056 (radium 223). However, 11-079 (XL-184) is about to open and accrual is expected to be brisk. Despite the phase I trials, UWash exceeded the annual minimum goal of 35 patients per year. See Supporting Document section (Table E) showing quarterly and total accrual figures to date for UWash.

Task 7. Enact a Plan for Accruing Patients from Disproportionately Affected Populations (DAP)

According to the 2010 census data from http://factfinder2.census.gov/faces/nav/jsf/pages/index.xhtml, Washington has a total population of 6.7 million yet has an African American population (AA) of only 3.6%. This is a much lower percentage of the total population than other states with PCCTC sites of similar size including Massachusetts (6.5 million, 6.6% AA), Maryland (5.8 million, 29.4% AA), and Wisconsin (5.7 million, 6.9% AA).

Minority accrual for the period 3/31/10-4/1/11 included 2 of 42 (4.7%) patients enrolled on therapeutic trials and 2 of 7 (29%) patients on biomarker studies.

Reaching disproportionately affected populations at risk for prostate cancer is a high priority for the FHCRC/University of Washington Cancer Consortium. The plan to reach out to DAP in the state of Washington includes the following strategies:

1. Attend local prostate cancer support groups to develop one-on-one contact with individuals from DAP. This year faculty members attended support groups in Bellevue, Tacoma, and Seattle.

2. Include members of DAP in our SPORE Advocates Committee. Members receive information about new clinical trials and other on-going scientific research at each meeting from a member of the research team. Currently, Willie Stewart who is also one of the US Too Support group leaders, reaches out to African American men through work with the American Cancer Society and through local churches.

3. Offer educational activities held on the Fred Hutchison Cancer Research Center campus to the lay public not only to educate, but also familiarize the public with the Seattle Cancer Care Alliance, our outpatient clinic facility on the campus. On October 9, 2010 we held our annual Pacific NW Prostate Cancer Conference in conjunction with Oregon Health Sciences University (flyer in Appendix B).

4. Demonstrate our institution's support of prostate cancer awareness activities sponsored by other groups. Last Fall, the clinical research staff attended the local PACE race with educational outreach materials. This race was held October 10, 2010 aimed to help increase awareness of prostate cancer and educate men and their families about treatment options for prostate cancer. The race is held in downtown Kirkland Washington, located on the eastside of King County. Dr. Higano "kicked off" the race with a motivational talk thanking the participants for their work to bring attention to prostate cancer. As well as, Dr. Higano, several staff participated in the PACE race itself. Dr. Yu, the research staff and other colleagues from FHCRC and our SPORE Advocacy Committee attended a "Pints for Prostates" event at the Pike Brewery on June 16, 2010 and at other locals on June 19, 2010 across King County. During November, several faculty members and Anna Singer (Dr. Higano's daughter) supported and participated in the "Movember" prostate cancer awareness moustache campaign.

5. Utilize the FHCRC Community Outreach Manager, Juan Cotto, who is also African American, to connect with other minority leaders and groups in the greater Seattle area to enhance awareness of prostate cancer and clinical trials and the importance of science education. In 2010, the Center made a video that introduces Juan, his story, and his role at http://www.fhcrc.org/science/education/livesofscience/profiles/cotto.html).

6. Work with network sites in areas where DAP have migrated. Demographic studies have shown that both minorities as well as those over age 65 have migrated from Seattle to outlying suburban areas, primarily due to the costs of real estate. UWash is working to expand appropriate trials to sub-investigators located at SCCA Network Affiliate partners in these locations, thus allowing minority patients greater access to prostate cancer clinical trials. On April 5, 2011 it was announced that Group Health Cooperative, a large HMO in Washington and northern Idaho covering over 674,900 residents, joined the SCCA Network. It is hope that this addition to the Network will further enhance our accrual of DAP in the coming years.

Task 8. Prepare Status Reports

UWash has prepared and submitted all required status reports, made oral presentations to the Integration Panel, and attended all Consortium meetings detailed above.

Task 9. Write Abstracts or Papers relevant to Consortium Trials

Publications

During period 4/1/10-3/31/11, investigators at UWash have been listed as authors on a total of 9 abstracts (all presented or to be presented at ASCO, AUA, AACR, or GU ASCO) and 2 manuscripts. A complete listing of abstracts and publications appears in References, and the UWash first authored abstracts themselves appear in the Appendix 3.

REFERENCES:

Listing of publications and presentations where UWash staff is an author during funding year (4/1/10-3/31/11)

A. UWash Consortium Publications in Peer-Reviewed Journals

1. Scher HI, Beer TM, Higano CS, Anand A, Taplin ME, Efstathiou E, Rathkopf D, Shelkey J, Yu EY, Alumkal J, Hung D, Hirmand M, Seely L, Morris MJ, Danila DC, Humm J, Larson S, Fleisher M, Sawyers CL; Prostate Cancer Foundation/Department of Defense Prostate Cancer Clinical Trials Consortium. Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study. Lancet. 2010 Apr 24;375(9724):1437-46. Epub 2010 Apr 14. PubMed PMID: 20398925.

2. Yu EY, Massard C, Gross M, Carducci M, Culine S, Hudes G, Posadas E, Sternberg C, Wilding G, Trudel G, Paliwal P, Fizazi K. Once-daily dasatinib: Expansion of a phase 2 study evaluating the safety and efficacy of dasatinib in patients with metastatic castration-resistant prostate cancer. Urology In Press

B. UWash Consortium Abstracts

1. Scher HI, Beer TM, Higano CS, Logothetis C, Taplin ME, Efstathious E, Hirmand M. Antitumor Activity of MDV3100 in a Phase 1-2 Study of Advanced Prostate Cancer. J Urol. April 2010; 183(4):e2627-e228. Presented at 2010 AUA Annual Meeting, May 29-June 3, 2010. Abstract #580.

2. Hotte SJ, Yu EY, Hirte HW, Higano CS, Gleave ME, Chi KN. Phase I Trial of OGX-427, a 2'methoxyethyl antisense oligonucleotide (ASO), Against Heat Shock Protein 27 (Hsp27): Final Results. J Clin Oncol. 2010, 28:7s. Abstract #3077.

3. Anand A, Scher HI, Beer TM, Higano CS, Danila DC, Taplin M, Efstathiou E, Hirmand M, Sawyers CL, Heller G. Circulating Tumor Cells (CTC) and Prostate Specific Antigen (PSA) as Response Indicator Biomarkers in Chemotherapy-Naïve Patients with Progressive Castration-Resistant Prostate Cancer (CRPC) Treated with MDV3100. J Clin Oncol. 2010, 28:7s. Abstract #4546.

4. Small EJ, Beer TM, Weinberg VK, Higano CS, Nordquist LT, Rosenberg JE, Alumkal JJ, Yu EY, Sun J, Lin AM. Intermittent Chemotherapy (Ich) for Metastatic Castration-Resistant Prostate Cancer (mCRPC): Results of a Prospective Randomized Phase II Trial of the DoD Prostate Cancer Clinical Trials Consortium. J Clin Oncol. 2010, 28:7s. Abstract #4684.

5. Hussain M, Rathkopf D, Liu G, Armstrong A, Kelly WK, Ferrari A, Hainsworth J, Yang L, Schwartz J, Youssougian H, Higano CS. A Phase 2 Randomized Study of Cixutumumab (IMC-A12) or Ramucirumab (IMC-1121B) Plus Mitoxantrone and Prednisone in Patients (pts) with Metastatic Castration Resistant Prostate Cancer (CRPC) Following Disease Progression on Docetaxel-Based Chemotherapy. DOD IMPaCT Conference, Orlando Florida, March 9-12, 2011.

6. Harzstark AL, Lin AM, Beer TM, Weinberg VK, Higano CS, Nordquist L, Rosenberg JE, Alumkal J, Yu EY, Mi J, Small EJ. Intermittent Chemotherapy (ICh) for Metastatic Castration Resistant Prostate Cancer (mCRPC): Results of a Prospective Randomized Phase 2 Trial of the DoD Prostate Cancer Clinical Trials Consortium. 2011 Submitted for GU ASCO.

7. Higano CS, Beer TM, Taplin ME, Efstathious E, Anand A, Hirmand M, Fleisher M, Scher HI, Prostate Cancer Clinical Trials Consortium. Antitumor Activity of MDV3100 in pre- and post-docetaxel advanced prostate cancer: Long-term follow-up of a Phase 1-2 Study. J Clin Oncol 29: 2011 (suppl 7; abstr 134)

8. Higano CS, Beer TM, Yu EY, Taplin M, Ewfstathiou E, Anad A, Hirmand M, Fleisher M, Scher HI, Prostate Cancer Clinical Trials Consortium. Long-term efficacy results from the phase 1-2 study of MDV3100 in pre- and post-docetaxel prostate cancer. *2011 Submitted for EAU.*

9. Higano C, True L, Morrissey C, Roudier M, Knudsen B, Montgomery B, Mostaghel E, Nelson P, Fligner C, Lange P, Vessella R. Clinical Characterisitcs of the University of Washington Tissue Acquisition at Necropsy Program in Prostate Cancer. Proceedings of the Second Innovative Minds in Prostate Cancer Today (IMPaCT) Conference, Orlando, Florida, March 9-12, 2011.

C. UWash Consortium Presentations

1. Evan Yu: Prostate Cancer Foundation Scientific Symposium: “Imaging prostate cancer bone metastases with sodium fluoride (NaF) PET.” Washington, DC. September 16, 2010.

2. Celestia Higano: PCCTC Accelerating the Development of Ipilimumab and Other Immunotherapy Approaches, Plenary Session, IMPaCT Meeting, Orlando, FLA, March 10, 2011 2011.

3. Celestia Higano: Androgen Deprivation: Understanding and Managing Toxicities, “Meet the Expert” Session, IMPaCT Meeting, Orlando, FLA, March 11, 2011.

Appendices

Appendix 1: Protocol Evaluation Form
Appendix 2: Community Symposia Flyer
Appendix 3: Publications

1. Scher HI, Beer TM,Higano CS, Logothetis C, Taplin ME, Efstathious E, Hirmand M. AntitumorActivity of MDV3100 in a Phase 1-2 Study of Advanced Prostate Cancer. J Urol. April 2010; 183(4):e2627-e228. Presented at 2010 AUA Annual Meeting, May29-June 3, 2010. Abstract #580.
2. Hotte SJ, Yu EY, Hirte HW, HiganoCS, Gleave ME, Chi KN. Phase I Trial of OGX-427, a 2'methoxyethylantisense oligonucleotide (ASO), Against Heat Shock Protein 27 (Hsp27): FinalResults. J Clin Oncol. 2010, 28:7s. Abstract #3077.
3. Anand A, Scher HI, Beer TM, HiganoCS, Danila DC, Taplin M, Efstathiou E, Hirmand M, Sawyers CL, Heller G. Circulating Tumor Cells (CTC) and Prostate Specific Antigen (PSA) as ResponseIndicator Biomarkers in Chemotherapy-Naïve Patients with ProgressiveCastration-Resistant Prostate Cancer (CRPC) Treated with MDV3100. J ClinOncol. 2010, 28:7s. Abstract #4546.
4. Small EJ, Beer TM, Weinberg VK,Higano CS, Nordquist LT, RosenbergJE, Alumkal JJ, Yu EY, Sun J, Lin AM. Intermittent Chemotherapy (Ich) forMetastatic Castration-Resistant Prostate Cancer (mCRPC): Results of aProspective Randomized Phase II Trial of the DoD Prostate Cancer ClinicalTrials Consortium. J Clin Oncol. 2010, 28:7s. Abstract #4684.
5. Hussain M, Rathkopf D, Liu G,Armstrong A, Kelly WK, Ferrari A, Hainsworth J, Yang L, Schwartz J, YoussougianH, Higano CS. A Phase 2 Randomized Study of Cixutumumab (IMC-A12) orRamucirumab (IMC-1121B) Plus Mitoxantrone and Prednisone in Patients (pts) withMetastatic Castration Resistant Prostate Cancer (CRPC) Following DiseaseProgression on Docetaxel-Based Chemotherapy. DOD IMPaCT Conference, Orlando Florida,March 9-12, 2011.
6. Harzstark AL, Lin AM, Beer TM,Weinberg VK, Higano CS, Nordquist L, Rosenberg JE, Alumkal J, Yu EY, Mi J,Small EJ. Intermittent Chemotherapy (ICh) for Metastatic Castration ResistantProstate Cancer (mCRPC): Results of a Prospective Randomized Phase 2 Trial ofthe DoD Prostate Cancer Clinical Trials Consortium. 2011 Submitted for GUASCO.
7. Higano CS, Beer TM,Taplin ME, Efstathious E, Anand A, Hirmand M, Fleisher M, Scher HI, ProstateCancer Clinical Trials Consortium. Antitumor Activity of MDV3100 in pre- andpost-docetaxel advanced prostate cancer: Long-term follow-up of a Phase 1-2Study. J Clin Oncol 29: 2011 (suppl 7; abstr 134)
8. Higano CS,Beer TM, Yu EY, Taplin M, Ewfstathiou E, Anad A, Hirmand M, Fleisher M, ScherHI, Prostate Cancer Clinical Trials Consortium. Long-term efficacy resultsfrom the phase 1-2 study of MDV3100 in pre- and post-docetaxel prostatecancer. 2011 Submitted for EAU.
9. Higano C, True L, Morrissey C,Roudier M, Knudsen B, Montgomery B, Mostaghel E, Nelson P, Fligner C, Lange P,Vessella R. Clinical Characterisitcs of the University of WashingtonTissue Acquisition at Necropsy Program in Prostate Cancer. Proceedings of the Second Innovative Minds in ProstateCancer Today (IMPaCT) Conference, Orlando, Florida, March 9-12, 2011.

APPENDIX 1 Date of Review:_____

University of Washington – Prostate Cancer Clinical Research Program
Protocol Evaluation Form

Basic design/population (protocol Attached):

Rate each section on a scale of 1-5

Reviewer:	Comments	Score
Scientific Interest 5 = High, novel and innovative 3 = Medium, interesting 1 = Low, no new science		
Potential Clinical Significance 5 = Excellent, results would change practice 3 = Medium, results will further advance clinical research 1 = Low, Results will have little/no clinical significance		
Protocol Design 5 = Excellent, no additional input 3 = Good ideas but design needs work 1 = Needs total design change		
Accrual/Eligibility Issues 5 = None, accrual will be easy 3 = Some potential accrual problems 1 = Will be extremely difficult to accrue to this trial		
Feasibility 5 = No foreseeable implementation issues 3 = Some potential implementation issues, but can be done 1 = Not feasible to implement protocol as it is now designed		
Intensiveness 5 = Not labor intensive 3 = Medium intensity 1 = Extremely labor intensive		
Exclusivity 5 = Only site participating 3 = Only NW site participating, small number of total sites 1 = Multiple trial sites and not exclusive Seattle site No. of sites participating: Other NW / Seattle sites:		
Competing Protocols 5 = No other competing protocols 3 = Some competing protocols, but minor differences in terms of population or treatment 1 = Multiple competing protocols for exact same treatment and/or population *List competing protocols:*		
Budget 5 = Generous budget 3 = Budget tight, but should be able to break even 1 = No financial support for trial		
Available Resources 5= plenty of resources available 3= resources tight 1= will need to hire resources or protocol has special needs		
Total:		

DOD or PCF credits? *Circle one*

Possible Correlative Studies (list):

Other Issues / Considerations / Comments:

Sponsored by

UNIVERSITY OF WASHINGTON

OREGON HEALTH & SCIENCE UNIVERSITY

FRED HUTCHINSON CANCER RESEARCH CENTER
A LIFE OF SCIENCE

LIVESTRONG SURVIVORSHIP CENTER OF EXCELLENCE NETWORK

10th Annual
Pacific NW
Prostate Cancer Conference

Saturday,
October 9, 2010
8:30 AM — 4:00 PM
Check in begins at 8:00 AM

Two Locations:

Fred Hutchinson Cancer Research Center
Seattle, WA
&
OHSU Knight Cancer Institute
Portland, OR

Join us for an educational day: hear state-of-the-art information on diagnosis, treatment and day-to-day issues for men living with prostate cancer.

Open to the public

Pre-registration is required as seating is limited

UNIVERSITY OF WASHINGTON

Pacific NW Prostate Cancer Conference
Seattle Cancer Care Alliance
825 Eastlake Ave E., G4-830
Seattle, WA 98109

October 9, 2010

For more information
visit our website at
www.UWprostatecancer.org
Or call 206/288-6269

10th Annual

Pacific NW Prostate Cancer Conference

Saturday, October 9, 2010

A message to our patients:

We consider you the most important member of your healthcare team and as such we invite you to attend this educational day and perhaps learn more about the research that's being done at our institutions as well as other institutions in the Pacific Northwest. You will have the opportunity to hear from leading experts in the field of prostate cancer, to meet local support group leaders and to ask questions of us and other speakers.

Please consider spending a Saturday with us and register early as seating is limited.

Agenda

Morning Session 8:30 AM

Welcome, Overview and Introductions
Tia Higano, MD, Tom Beer, MD

Patient Reported Outcomes
John Gore, MD

Translational Research (and broccoli!)
Joshi Alumkal, MD

Protecting Bone for Prostate Cancer Patients
Evan Yu, MD

Break: 20 minutes

Current Clinical Trials
Tia Higano, MD

New Treatments on the Horizon
Tom Beer, MD

Q&A panel for morning session
Lunch: 12:00 pm - 1:00 pm

—

Patient Education, Advocacy & Support
Jim Kiefert—Seattle Ridge Taylor— Portland

PAR for Life
Evan Denhart

Update on approaches to diagnosis and treatment
Dan Lin, MD

PCa Toolkit and Strategies
Sylvie Aubin, PhD

Fad diets and dietary supplements for prostate cancer. What works and what doesn't?
Mark Moyad, MD

Agenda is subject to changes unforeseen at time of printing

Speakers

Joshi Alumkal, MD
Oregon Health & Science
Sylvie Aubin, Ph.D.
McGill University
Tomaz Beer, MD
Oregon Health & Science
Evan Denhart
PAR for Life
John Gore
University of Washington
Tia Higano, M.D.
University of Washington
Jim Kiefert, Ed.D.
US TOO
Dan Lin, M.D.
University of Washington
Mark Moyad, M.D., M.P.H.
University of Michigan Medical Center
Author of *ABC's of Prostate Cancer*
Ridge Taylor
US TOO
Evan Yu, M.D.
University of Washington

TWO Locations:

Fred Hutchinson Cancer Research Center
Pelton Auditorium
1100 Fairview Ave N
Seattle, WA

Oregon Health & Science University
Knight Cancer Institute
3303 SW Bond Ave
Portland, OR

3 ways to register:

website: **http://www.UWprostatecancer.org**
By phone: **206-288-6269**
By E-mail: **suehall@ u.washington.edu**

ANTITUMOUR ACTIVITY OF MDV3100 IN CASTRATION-RESISTANT PROSTATE CANCER: A PHASE 1-2 STUDY.

Scher HI, Beer TM, Higano CS, Anand A, Taplin ME, Efstathiou E, Rathkopf D, Shelkey J, Yu EY, Alumkal J, Hung D, Hirmand M, Seely L, Morris MJ, Danila DC, Humm J, Larson S, Fleisher M, Sawyers CL; Prostate Cancer Foundation/Department of Defense Prostate Cancer Clinical Trials Consortium.

Background: MDV3100 is an androgen-receptor antagonist that blocks androgens from binding to the androgen receptor and prevents nuclear translocation and co-activator recruitment of the ligand-receptor complex. It also induces tumour cell apoptosis, and has no agonist activity. Because growth of castration-resistant prostate cancer is dependent on continued androgen-receptor signalling, we assessed the antitumour activity and safety of MDV3100 in men with this disease.

Methods: This phase 1-2 study was undertaken in five US centres in 140 patients. Patients with progressive, metastatic, castration-resistant prostate cancer were enrolled in dose-escalation cohorts of three to six patients and given an oral daily starting dose of MDV3100 30 mg. The final daily doses studied were 30 mg (n=3), 60 mg (27), 150 mg (28), 240 mg (29), 360 mg (28), 480 mg (22), and 600 mg (3). The primary objective was to identify the safety and tolerability profile of MDV3100 and to establish the maximum tolerated dose. The trial is registered with ClinicalTrials.gov, number NCT00510718.

Findings: We noted antitumour effects at all doses, including decreases in serum prostate-specific antigen of 50% or more in 78 (56%) patients, responses in soft tissue in 13 (22%) of 59 patients, stabilised bone disease in 61 (56%) of 109 patients, and conversion from unfavourable to favourable circulating tumour cell counts in 25 (49%) of the 51 patients. PET imaging of 22 patients to assess androgen-receptor blockade showed decreased (18)F-fluoro-5alpha-dihydrotestosterone binding at doses from 60 mg to 480 mg per day (range 20-100%). The median time to progression was 47 weeks (95% CI 34-not reached) for radiological progression. The maximum tolerated dose for sustained treatment (>28 days) was 240 mg. The most common grade 3-4 adverse event was dose-dependent fatigue (16 [11%] patients), which generally resolved after dose reduction.

Interpretation: We recorded encouraging antitumour activity with MDV3100 in patients with castration-resistant prostate cancer. The results of this phase 1-2 trial validate in man preclinical studies implicating sustained androgen-receptor signalling as a driver in this disease.

FUNDING: Medivation, the Prostate Cancer Foundation, National Cancer Institute, the Howard Hughes Medical Institute, Doris Duke Charitable Foundation, and Department of Defense Prostate Cancer Clinical Trials Consortium.

PHASE I TRIAL OF OGX-427, A 2'METHOXYETHYL ANTISENSE OLIGONUCLEOTIDE (ASO), AGAINST HEAT SHOCK PROTEIN 27 (HSP27): FINAL RESULTS.

S. J. Hotte, E. Y. Yu, H. W. Hirte, C. S. Higano, M. E. Gleave, K. N. Chi; Juravinski Cancer Centre, Hamilton, ON, Canada; University of Washington, Seattle, WA; University of Washington School of Medicine, Seattle, WA; Vancouver Prostate Centre, Vancouver, BC, Canada; Vancouver Cancer Center, BC Cancer Agency, Vancouver, BC, Canada

Background: Hsp27 is a chaperone protein that affects multiple pathways implicated in cancer progression and treatment resistance. OGX-427 is a 2nd generation ASO that inhibits Hsp27 expression resulting in cell growth inhibition, apoptosis, and enhanced chemotherapy efficacy. The purpose of this study was to determine the safety profile and Phase 2 dose of OGX-427 alone and in combination with docetaxel (D).

Methods: Eligible patients (pts) had metastatic castrate resistant prostate cancer (CRPC), breast, non-small cell lung (NSCLC), or ovarian cancer. OGX-427 was administered IV weekly on a 21-day schedule after 3 loading doses. OGX-427 was escalated over 5 planned dose levels (DL) (200-1,000 mg) and OGX-427+D (75mg/m2) over 2 DL (800 and 1,000 mg) with 6 pts/DL.

Results: 36 pts were treated with OGX-427 and 12 with OGX-427+D. Median age was 62 (33-86) yrs ; 27 pts had CRPC, 11 breast, 5 ovary and 5 NSCLC ; median prior chemotherapy regimens was 3 (0-6). 1 pt had dose-limiting toxicity with a grade 3 cerebral bleed into a metastasis. Of 556 infusions, 1 dose needed modification for toxicity. Infusion reactions (rigors, pruritus, flushing, back pain, dyspnea) were seen at DL ≥600 mg (interruption 14 pts, discontinuation 5 pts). PTT transiently increased to ≥ twice pretherapy levels at Cmax in 71% pts at DL≥ 800mg. The most common serious adverse events were dyspnea (5) and hydronephrosis/high creatinine (2). In pts with measurable disease, 4/30 given OGX-427 had a confirmed minor response or stable disease (SD) as best response and, of 7 pts with CRPC given OGX-427+D, 2 had a partial response and 1 SD for 7 months. PSA declines of ≥30% were seen in 3/16 (OGX-427) and 5/9 (OGX-427+D) evaluable pts. Of 41 pts with total or Hsp27+ circulating tumor cell (CTC) counts >5 at baseline, 10/32 (OGX-427) and 5/9 (OGX-427+D) pts decreased to ≤5.

Conclusions: OGX-427 at the maximum doses tested of 1,000 mg was well tolerated and combination with D was feasible. Toxicity consisted mainly of infusion reactions and transient PTT changes. Changes in tumor markers, measurable disease, and CTC suggested single-agent activity. Further study of OGX-427 alone and in combination with D is planned.

CIRCULATING TUMOR CELLS (CTC) AND PROSTATE SPECIFIC ANTIGEN (PSA) AS RESPONSE INDICATOR BIOMARKERS IN CHEMOTHERAPY-NAÏVE PATIENTS WITH PROGRESSIVE CASTRATION-RESISTANT PROSTATE CANCER (CRPC) TREATED WITH MDV3100.

A. Anand, H. I. Scher, T. M. Beer, C. S. Higano, D. C. Danila, M. Taplin, E. Efstathiou, M. Hirmand, C. L. Sawyers, G. Heller, Prostate Cancer Clinical Trials Consortium; Memorial Sloan-Kettering Cancer Center, New York, NY; Oregon Health & Science University Knight Cancer Institute, Portland, OR; University of Washington School of Medicine, Seattle, WA; Dana-Farber Cancer Institute, Boston, MA; University of Texas M. D. Anderson Cancer Center, Houston, TX; Medivation, Inc., San Francisco, CA

Background: The availability of reliable indicators of treatment efficacy is a critical unmet need in drug development for CRPC. MDV3100 is a second-generation oral androgen receptor antagonist that induces a prolonged apoptotic response in xenograft models and is active in men with progressive CRPC. We explored outcomes based on PSA and CTC number in relation to radiographic progression.

Methods: 65 chemotherapy-naive patients with progressive CRPC were treated at doses of 30 to 360 mg/day. PSA levels were measured monthly, and CTC number at baseline, wks 4 and 12 using the Cell Search assay. A "PSA response" was defined as 3 consecutive declines within 12 wks of the start of treatment. Time to radiographic progression free survival (RPFS) was assessed by Prostate Cancer Working Group 2 criteria. The likelihood ratio test from the Cox proportional hazards model was used to determine the factors associated with RPFS, defined as being alive without progression.

Results: The RPFS probability at 12 months was 0.56 (95% CI: 0.43, 0.73) with a median follow up of 13 months (2.4 to 26). 48 (74%) of the 65 pts were evaluable at the 12 wk landmark. CTC number, PSA, and PSA response, all assessed at 12 weeks, were all significant predictors of RPFS ($p < 0.001$). The joint model most predictive of RPFS time was CTC at 12 weeks and PSA response (3 consecutive declines). The concordance probability estimate (CPE) was used to measure the predictive accuracy of the model. The CPE for this joint model was 0.78, significantly higher than a model with each factor alone (CTC at 12 weeks - CPE= 0.63; PSA response- CPE=0.72).

Conclusions: CTC at 12 weeks and PSA response provide independent predictive information for radiographic progression free survival time in chemotherapy-naive CRPC. Sustained PSA declines are consistent with the observed preclinical apoptotic response. Each biomarker may provide unique information. The results will be studied prospectively in an ongoing phase III randomized trial of MDV3100 with a survival endpoint.

INTERMITTENT CHEMOTHERAPY (ICH) FOR METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC): RESULTS OF A PROSPECTIVE RANDOMIZED PHASE II TRIAL OF THE DOD PROSTATE CANCER CLINICAL TRIALS CONSORTIUM

E. J. Small, T. M. Beer, V. K. Weinberg, C. S. Higano, L. T. Nordquist, J. E. Rosenberg, J. J. Alumkal, E. Y. Yu, J. Sun, A. M. Lin; University of California, San Francisco, San Francisco, CA; Oregon Health & Science University Knight Cancer Institute, Portland, OR; University of Washington School of Medicine, Seattle, WA; Oncology Hematology West PC, Omaha, NE; Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA; Oregon Health & Science University, Portland, OR; University of Washington, Seattle, WA

Background: Docetaxel remains the standard of care for patients (pts) with mCRPC. However the optimal duration of chemotherapy (Ch) is not known. Providing Ch holidays is often undertaken, but not well characterized. A randomized phase II trial was undertaken to test two ICh regimens.

Methods: Pts with Ch naive mCRPC and KPS > 60% were eligible. Pts were treated with "induction" docetaxel 75 mg/m2 q 3 weeks, and prednisone 5 mg po bid. After 6 cycles, responding pts (PSAWG1 criteria) stopped Ch and were randomized to observation (Obs) or to GM-CSF, 250 mcg/m2 sq daily for 14 days out of every 28 day cycle. Pts were followed with monthly PSA and imaging every 2 cycles until progressive disease (PD) by PSAWG1 criteria, at which point they resumed treatment with Ch, again for 6 cycles, followed by the same "off Ch" regimen. The primary endpoint was the time to PD while on Ch (time to Ch resistance).

Results: Of 66 enrolled pts to date, 58 are evaluable (8 are still undergoing induction). 41 pts completed induction (17 did not due to PD, adverse events (AE), or MD choice), of which 14 had PD after 6 cycles. Thus, 27/58 evaluable pts (47%) were eligible for randomization. Of these, 14 pts underwent Obs and 13 received GM-CSF. To date, 16/27 (59%) pts who underwent a Ch holiday restarted Ch, all for PSA PD. 4/16 had a response to Ch re-initiation. (8 pts did not re-start Ch because of AE or other therapy being started, and 3 pts are still undergoing either Obs or GM-CSF.) Obs pts were "off Ch" for 29% of the total cycle time, compared with 42.5% for GM-CSF pts.

Conclusions: While feasible, only 47% of pts met criteria for ICh. 25% of pts responded to Ch re-initiation. Insufficient data exist to assess the impact of GM-CSF on time off Ch or time to Ch resistance.

A PHASE 2 RANDOMIZED STUDY OF CIXUTUMUMAB (IMC-A12) OR RAMUCIRUMAB (IMC-1121B) PLUS MITOXANTRONE AND PREDNISONE IN PATIENTS (PTS) WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER (CRPC) FOLLOWING DISEASE PROGRESSION ON DOCETAXEL-BASED CHEMOTHERAPY

M Hussain[1,10], D Rathkopf[2,10], G Liu[3,10], A Armstrong[4,10], WK Kelly[5], A Ferrari[6], J Hainsworth[7], L Yang[8], J Schwartz[8], H Youssougian[8], C Higano[9,10].
[1]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; [2]Memorial Sloan-Kettering, New York, NY; [3]University of Wisconsin, Madison, WI; [4]Genitourinary Oncology Research Program, Durham, NC; [5]Yale Cancer Center, New Haven, CT; [6]New York University Clinical Cancer Center, New York, NY; [7]Sarah Cannon Cancer Center, Nashville, TN; [8]ImClone Systems a wholly-owned subsidiary of Eli Lilly and Company, Branchburg, NJ; [9]University of Washington, Fred Hutchinson Cancer Research Center, Seattle, WA; [10]Members of the Prostate Cancer Clinical Trials Consortium (PCCTC), a program of the Prostate Cancer Foundation and the Department of Defense Prostate Cancer Research Program (DOD PCRP)

Background: Vascular endothelial growth factor (VEGF)-mediated angiogenesis and insulin-like growth factor (IGF-1R)-mediated signaling contribute to prostate cancer progression. Cixutumumab (CIX; IMC-A12) is a fully human IgG1 recombinant monoclonal antibody (MAb) that specifically targets the human IGF-IR and ramucirumab (RAM; IMC-1121B) is a fully human IgG1 MAb that inhibits VEGF receptor-2 (VEGFR-2) binding and signaling. We investigated the safety and efficacy of CIX or RAM in combination with mitoxantrone (M) plus prednisone (P) in CRPC pts that had progressive disease (PD) on docetaxel.

Methods: Eligible pts had metastatic CRPC with PD during/within 120 days of docetaxel (defined as PD by RECIST, at least 2 new bone lesions, and/or increasing PSA), ECOG PS 0-2, PSA ≥ 2 ng/mL, and adequate organ function. All pts received M 12 mg/m^2 IV on day 1 every 3 weeks + P 5 mg PO BID and were randomized to either CIX 6 mg/kg or RAM 6 mg/kg each administered IV weekly for up to 12 cycles. Tumor assessments were after the first 3 cycles then q6w. The primary endpoint was composite progression-free survival (cPFS, as defined by RECIST, bone scan progression, new skeletal events, and other components, including death). Other endpoints were safety, response, overall survival (OS), and pharmacokinetic/pharmacodynamic profiles. Sample size was based on a targeted 50% improvement in median cPFS from 11.1 to 16.7 weeks, based on results presented from a large trial in chemotherapy refractory CRPC in which a similar cPFS was employed (SPARC; Sternberg et al. ASCO 2007).

Results: Of 139 pts randomized, 132 received study treatment. The median age for the 66 pts on CIX was 65yr and for the 66 pts on RAM 68 yrs. The median PSA for CIX was 118.5 ng/mL and 113.8 ng/mL for RAM. Median number of cycles were 5 for CIX and 6 for RAM. Median duration of follow-up was 6.8 months (m) for CIX and 9.1m for RAM. 19 pts continue to receive RX as of 7-29-10. The most frequently observed AEs considered at least possibly related to study drug: for CIX included fatigue 59% (15% Grade [G] ≥3), nausea 38% (2% G≥3), and anorexia 33% (0 G≥3); for RAM included fatigue 58% (5% G≥3), nausea 35% (0 G≥3), and diarrhea 30% (2% G≥3). Preliminary median cPFS is 4.1m (2.2-6.3m 95% CI) on CIX and 7.4m (4.5-9.3m 95% CI) on RAM. Preliminary OS is 10.2m (6.4-15.4m 95% CI) on CIX and 13.0m (9.3-16.7m 95% CI) on RAM. Preliminary PSA response is the same for both arms at 21% (11-34% 95% CI). Preliminary radiographic response rate (CR+PR) is 9.1% (3.4-18.7% 95%CI) on CIX and 10.6% (4.4-20.6% 95% CI) on RAM.

Conclusions: Both CIX/M/P and RAM/M/P were reasonably tolerated in CRPC. Preliminary PFS and OS of RAM/M/P appear encouraging, favoring further investigation of this regimen.

Impact: Therapeutic options in chemotherapy refractory prostate cancer are limited. The protocol investigates two novel regimens involving targeted monoclonal antibodies in combination with an established cytotoxic chemotherapy in patients with docetaxel-refractory, castrate resistant prostate cancer. The addition of an anti-VEGFR2 antibody therapy to mitoxantrone/prednisone appears encouraging and may be associated with enhanced efficacy and a favorable safety profile.

Acknowledgement: Drs' Hussain, Rathkopf, Liu, Armstrong and Higano are supported by the DOD PCRP and the Prostate Cancer Foundation.

INTERMITTENT CHEMOTHERAPY (ICH) FOR METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC): RESULTS OF A PROSPECTIVE RANDOMIZED PHASE II TRIAL OF THE DOD PROSTATE CANCER CLINICAL TRIALS CONSORTIUM.

A. L. Harzstark, T. M. Beer, V. K. Weinberg, C. S. Higano, L. T. Nordquist, J. E. Rosenberg, J. J. Alumkal, E. Y. Yu, J. Mi, E. J. Small; University of California, San Francisco, San Francisco, CA; Oregon Health and Science University Knight Cancer Institute, Portland, OR; University of Washington School of Medicine, Seattle, WA; Oncology Hematology West PC, Omaha, NE; Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA; University of Washington, Seattle, WA

Background: Docetaxel remains the standard of care for patients (pts) with mCRPC. However, the optimal duration of chemotherapy (Ch) is not known. Providing Ch holidays is often undertaken, but is not well characterized. A randomized phase II trial was undertaken to test two ICh regimens.

Methods: Pts with Ch naive mCRPC and KPS > 60% were eligible. Pts were treated with "induction" docetaxel 75 mg/m2 q3 weeks, and prednisone 5 mg po bid. After 6 cycles, responding pts (PSAWG1 criteria) stopped Ch and were randomized to observation (Obs) or to GM-CSF, 250 mcg/m2 sq daily for 14 days out of every 28 day cycle. Pts were followed with monthly PSA and imaging every 2 cycles until progressive disease (PD) by PSAWG1 criteria, at which point they resumed treatment with Ch, again for 6 cycles, followed by the same "off Ch" regimen. The primary endpoint was the time to PD while on Ch (time to Ch resistance.)

Results: Of 97enrolled pts to date, 94 are evaluable (3 are still undergoing induction). 69 pts completed induction (25 did not due to PD, adverse events (AE), or MD choice), of which 27 had PD after 6 cycles. Thus, 42/94 evaluable pts (45%) were eligible for randomization. Of these, 21 pts underwent Obs and 21 received GM-CSF. To date, 23/42 (55%) pts who underwent a Ch holiday restarted Ch, all for PSA PD. 8/23 (35%) had a response to Ch re-initiation. (15 pts did not re-start Ch because of AE, other therapy being started, or patient choice, and 4 pts are still undergoing either Obs or GM-CSF.) Obs pts were "off Ch" for a median of 2 months (range 2-4), compared with 3 months (range 2-8) for GM-CSF pts.

Conclusions: While feasible, only 45% of pts met criteria for ICh. 35% of pts responded to Ch re-initiation. Insufficient data exist to assess the impact of GM-CSF on time off Ch or time to Ch resistance.

ANTI-TUMOR ACTIVITY OF MDV3100 IN PRE- AND POST-DOCETAXEL ADVANCED PROSTATE CANCER: LONG-TERM FOLLOW-UP OF A PHASE 1/2 STUDY.

C.S. Higano, T. M. Beer, M. E. Taplin, E. Efstathiou, A. Anand, M. Hirmand, M. Fleisher, H. I. Scher, Prostate Cancer Clinical Trials Consortium; University of Washington School of Medicine, Seattle, WA; Oregon Health & Science University Knight Cancer Institute, Portland, OR; Dana-Farber Cancer Institute, Boston, MA; University of Texas M. D. Anderson Cancer Center, Houston, TX; Memorial Sloan-Kettering Cancer Center, New York, NY; Medivation, Inc., San Francisco, CA; Sidney Kimmel Center for Prostate and Urologic Cancers, New York, NY

Background: MDV3100 is a novel androgen receptor (AR) antagonist selected for potent AR activity and devoid of partial agonist effects. A preliminary report of the Phase 1/2 study described anti-tumor activity and adverse events (Scher HI et al. Lancet. 2010; 375:1437). This abstract provides long-term follow-up on time to PSA and radiographic progression in this trial.

Methods: Patients (pts) with progressive castration resistant prostate cancer (CRPC) were enrolled in sequential cohorts of 3 - 6 pts at MDV3100 doses of 30, 60, 150, 240, 360, 480 and 600mg/day. Once the tolerability of a dose was established, enrollment was expanded at doses ≥60mg/day to include approximately 12 chemotherapy naïve (naïve) pts and 12 pts previously treated with docetaxel (post-chemo) per cohort.

Results: 140 pts were enrolled of which 18 (13%) pts continue on active treatment (16 naive and 2 post-chemo). The median time on treatment is 51 weeks for naïve and 17 weeks for post-chemo groups. Median time on treatment for the 18 patients still on study is 131 weeks. The median time to PSA progression, defined per-protocol as a ≥25% increase in PSA from baseline, was not met for naïve and was 33 weeks for post-chemo groups. Median time to PSA progression by Prostate Cancer Clinical Trials Working Group 2 criteria was 41 weeks for naïve and 20 weeks for post-chemo groups. Median time to radiographic progression was 56 weeks for naïve and 24 weeks for post-chemo groups. Circulating tumor cell counts available for128 of 140 pts showed 91% (70/77) with favorable pre-treatment counts (<5 cells/7.5mL blood) remaining favorable post-treatment, while 49% (25/51) converted from unfavorable pre-treatment to favorable post-treatment.

Conclusions: MDV3100 demonstrates durable anti-tumor activity in pts with CRPC both before and after chemotherapy. Based on these promising results MDV3100 is currently being evaluated in two global Phase 3 studies in pts with metastatic CRPC, the AFFIRM study in pts previously treated with docetaxel and the PREVAIL study in chemotherapy-naïve pts who have progressed on androgen deprivation therapy.

LONG-TERM EFFICACY RESULTS FROM THE PHASE 1-2 STUDY OF MDV3100 IN PRE- AND POST-DOCETAXEL ADVANCED PROSTATE CANCER

Celestia S. Higano,[1] Tomasz M. Beer,[2] Evan Yu[1], Mary-Ellen Taplin,[3] Eleni Efstathiou,[4] Aseem Anand,[5] Mohammad Hirmand,[6] Martin Fleisher,[5] Howard I. Scher,[5] and The Prostate Cancer Clinical Trials Consortium. [1]University of Washington School of Medicine, Fred Hutchinson Cancer Research Center, Seattle, WA; [2]Oregon Health & Science University, Portland, OR; [3]Dana-Farber Cancer Institute, Boston, MA; [4]University of Texas M. D. Anderson Cancer Center, Houston, TX; [5]Memorial Sloan-Kettering Cancer Center, New York, NY; 6Medivation, Inc., San Francisco, CA

Introduction: MDV3100 is a novel androgen receptor (AR) antagonist selected for its activity against prostate cancer (PCa) cells that overexpress AR. In pre-clinical models, MDV3100 slows growth and induces cell death in bicalutamide-resistant tumors via three complementary actions – on AR–direct antagonism, inhibition of nuclear translocation of the AR complex, and inhibition of the AR from binding to DNA (Tran C et al. Science. 2009;324:787). MDV3100 is devoid of AR agonist activity in vitro. In patients, preliminary antitumor activity and adverse events have been reported in advanced PCa from a phase 1-2 study of MDV3100 (Scher HI et al. Lancet. 2010;375:1437). Long-term follow-up for time to prostate-specific antigen (PSA) and radiographic progression from this study are presented.

Methods: Patients with progressive castration-resistant PCa (CRPC) were enrolled in sequential cohorts of 3 to 6 patients of MDV3100 doses of 30, 60, 150, 240, 360, 480, and 600 mg/day. After confirming dose tolerability, enrollment was expanded for doses ≥60 mg/day to include approximately 24 patients (n = 12/group) per cohort who were either chemotherapy-naïve (naïve) or previously treated with docetaxel (post-chemo).

Results: In total, 140 patients were enrolled, 18 (13%) of whom continue on active treatment (naïve, n = 16; post-chemo, n = 2) a median of 131 weeks after starting therapy. Long-term follow-up results are presented below:

	Naïve patients	Post-chemo patients
Median time on treatment	51 weeks	17 weeks
Median time to PSA progression (defined as a ≥25% increase in PSA from baseline)	Not Reached	33 weeks
Median time to PSA progression (Prostate Cancer Working Group 2 definition)	41 weeks	20 weeks
Median time to radiographic progression	56 weeks	24 weeks

CTC counts were available in 128 of 140 patients of whom 91% (70/77) of patients with favorable pre-treatment circulating tumor cell (CTC) counts (ie, <5 cells/7.5 mL blood) remained favorable post-treatment, whereas 49% (25/51) converted from unfavorable pre-treatment status to favorable post-treatment status.

Conclusions: In this phase 1 - 2 study, MDV3100 demonstrated durable antitumor activity in chemo-naïve and post-chemo patients with CRPC. To confirm these promising results, MDV3100 is being evaluated in 2 ongoing global phase 3 studies in patients with advanced progressive PCa: the AFFIRM study in patients previously treated with docetaxel, and the PREVAIL study in asymptomatic or mildly symptomatic chemotherapy-naïve patients who have progressed following androgen deprivation therapy.

CLINICAL CHARACTERISITCS OF THE UNIVERSITY OF WASHINGTON TISSUE ACQUISITION AT NECROPSY PROGRAM IN PROSTATE CANCER.

Celestia Higano, Lawrence True, Colm Morrissey, Martine Roudier, Beatrice Knudsen, Bruce Montgomery, Elahe Mostaghel, Pete Nelson, Corrine Fligner, Paul Lange, Robert Vessella. University of Washington School of Medicine, Fred Hutchinson Cancer Research Center, Seattle, Washington

Background: The University of Washington Tissue Acquisition at Necropsy (TAN) Program was initiated in 1991. The aim of this program was to obtain prostate cancer tissue to raise xenograft cell lines and to store tissue from both primary and metastatic sites for further study. In 1997 a systematic approach to bone biopsies was added whereby biopsies from 20 pre-defined bone sites were acquired and starting in 1998, patients were also consented for formal autopsy in addition to the TAN.

Methods: Patients or their next of kin signed informed consent to participate in the TAN program +/- formal autopsy. Within 2-4 hours of death, the body was transported to the University of Washington where the TAN team harvested and prepared tissue as previously described. Formal autopsy was conducted on the next business day.

Results: As of December 2010, 99 patients signed informed consent to participate in the TAN program. Twelve patients had harvest of only visible tissue (T) while, after 1997 41 had tissue and bone (TB) harvested and 46 had harvest of tissue, bone, and formal autopsy (TBA). The median age of all patients at diagnosis was 63 years (range 42 -93) and at death was 72 years (45.7-93). There were 94 Caucasians, 4 Asians, and 1 African American. At diagnosis 41 had local disease, 22 had regional disease (D1), 34 had metastases, and 2 were unknown; the median time from diagnosis to death was 9, 5, 3, and 17 years respectively. Of the 46 TBA patients, sites of disease included: bone 100%, lymph node 78%, lung 46%, liver 44%, adrenal 26%, pleura 22%, kidney 11%, pancreas 9%, spleen 9%, leptomeniges 6%, brain 3%. All patients were treated with at least one hormonal therapy and 66 patients (67%) received at least one chemotherapy regimen. All patients had end-stage prostate cancer at the time of death and died due to prostate cancer or due to contributing co-morbidities such as bacterial meningitis, pneumonia, intestinal obstruction, cerebral vascular accident, disseminated nocardia, and disseminated cryptococcus. Eleven of the total 24 xenograft cell lines raised in our lab derived from the TAN program since 1991 and over 1500 bone specimens and 350 non-bone samples have been collected.

Conclusion: The challenge of obtaining metastatic tissues from living patients led to the establishment of the TAN program at UW. In addition to the production of LuCaP xenograft lines which have been sent to over 100 investigators world wide, the TAN program has yields valuable metastatic bone and tissue samples which are fully annotated with disease characteristics, treatment and outcomes data. It is hoped that interrogation of these tissues will further define subtypes of prostate cancer and prognostic/predictive biomarkers in an effort to better personalize treatment options for each patient.

Supporting Data

Table A:	Trials Introduced by the University of Washington (02/11/07-03/31/11)
Table B:	Trials in Which the University of Washington Participated (02/11/07-03/31/11)
Table C:	Correlative Samples Collected at University of Washington
Table D:	PCWG2 Bone Scan Worksheet Collected at University of Washington (This budget period and cumulative through March 2011)
Table E:	Quarterly Patient Accrual by the University of Washington from 02/11/07 through 03/31/11

SUPPORTING DATA

University of Washington

Table A: Correlative samples collected at Un iversity of Washington (4/1/10-3/31/11)

Study	Description of samples collected	Number of samples collected (04/1/10 –03/31/11)
C06-012 UCSF	❖ Serum ❖ Plasma	**12**
C07-008 OGX-427	❖ Pharmacokinetic ❖ Hsp27 (serum and EDTA) ❖ Split complement ❖ CTC	**27**
C07-015 MDV 3100	❖ Pharmacokinetic ❖ CTC ❖ N-telopeptide ❖ Bone-specific alk phos	**18**
C08-005 HE-3235	❖ Pharmacokinetics ❖ Banked serum samples (eg ACTH) ❖ CRP ❖ PAP ❖ CTC	**16**
09-046 TOK-001	❖ Pharmacokinetic ❖ Deoxycortisol, corticosterone, cortisol, pregneolone ❖ 17alpha hydroxyprogesterone ❖ Dehydroepiandrosterone ❖ Deoxycorticosterone ❖ Androstenedrone	**108**
09-039 Kinex ph I/II	❖ Pharmacokinetics ❖ Ionized Calcium ❖ N-telepeptide ❖ C-telopeptide ❖ Bone-specific alk phos ❖ Circulating Tumor Cell enumeration and characterization ❖ Osteocalcin ❖ VEGF ❖ Phospor SRC-TYR ❖ TMPRSS-ERG ❖ PSA (KLK3, KLK2)	**172**
10-060 MLN ph I/I	❖ Docetaxel and MLN 8237 Pharmacokinetics ❖ Gynotypying ❖ aurorA kinase ❖ beta III tubulin	**178**
TOTAL		**531**

*** Cumulative correlative samples collected since our initial funding year of 2007 is 3,423 samples across various PCCTC trials*

Table B: PCWG2 Bone Scan Worksheet collected at University of Washington (this budget period and cumulative through March 2011)

Study	Number of Patients with assessments this budget period	Number of Assessments this budget period	Cumulative Number of Assessments
b10-001 (BMS ph III)	3	16	16
b09-003 (MDV 3100 ph III)	4	8	12
b09-002 (COU 301 ph III)	1	12	15
b09-005 (COU 302 ph III)	14	31	80
c09-039 (Kinex ph I/II)	4	12	12
c10-060 (MLN ph I/II)	4	9	9
Total	**40**	**88**	**144**

Table C: Trials Introduced by the University of Washington and currently active (2/11/07- 03/31/11)

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			PI	Participating Sites	Comments
				IRB approval	Open to accrual	Closed to accrual			
c07-002	Multicenter, Double-Blind Study Comparing 0.5 mg Dutasteride vs. Placebo Daily in Men Receiving Intermittent Androgen Ablation Therapy for Prostate Cancer	100	10/97	12/06	4/07	9/09	Higano	OHSU UBC CURC sites	Enrollment Complete, pts remain on treatment and in followup
c07-007	Phase II Single Arm, Open-Label Study of IMC-A12 in Asymptomatic, Chemotherapy-Naive Patients with Metastatic Androgen-Independent Prostate Cancer	41	17/24	7/07	8/07	2/09	Higano	UCSF OHSU	Enrollment Complete, pts remain on treatment and in followup
c07-008	A Phase I Study Evaluating a Second Generation Antisense Oligonucleotide (OGX-427) that Inhibits Heat Shock Protein 27 (Hsp27)	Up to 64	27/65	6/07	6/07	10/10	Yu	UBC Outside sites	Enrollment Complete (9/2010), pts remain on treatment and in followup
c08-005	A Phase II Open-Label Dose-Ranging Study of the Safety, Tolerance, Pharmacokinetics, and Potential Activity of HE3235 when Administered Orally to Patients with Prostate Cancer	Up to 64	8/51	7/08	7/08	12/10	Mont-gomery	MSKCC UCSF Outside sites	Enrollment Complete (12/2010), pts remain on treatment and in followup

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			PI	Participating Sites	Comments
				IRB approval	Open to accrual	Closed to accrual			
c08-015	Evaluation of 18f-fluoride PET as a Pharmacodynamic Biomarker for Dasatinib, a Src Kinase Inhibitor, in Men with Prostate Cancer and Bone Metastases	Up to 24	13/17	10/09	10/09	NA	Yu	FCC, Duke, MD Anderson, OHSU, UCSF	Enrollment on hold in 11/2010 for main treatment trial
c09-046	Phase 1/2, Open Label, Dose Escalation, Selected Dose Comparison Trial of Tok-001 for the Treatment of Chemotherapy Naïve Castration Resistant Prostate Cancer	50	4/49	12/09	12/09	N/A	Mont-gomery	DFCC	Enrolls in small dosing cohorts
c10-060	A Randomized Phase 2 Study of MLN8237, an Aurora A Kinase Inhibitor, or No MLN8237 in Patients with Castration Resistant Prostate Cancer Receiving a Standard Docetaxel/Prednisone Regimen, Preceded by a Phase 1 Dose-Escalation Study	118	4/9	4/10	pending	N/A	Higano	OHSU	Enrolls in small dosing cohorts
c11-0081	Phase II Study of Single Agent OGX-427 in Asymptomatic Metastatic Castration Resistant Prostate Cancer Prior to Docetaxel Therapy	32	0/6	pending	pending	N/A	Yu	OHSU	Expected to open 6/11

Table D: Trials in Which the University of Washington Participated or there was significant activity (4/1/2010-3/31/11)

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			In-House PI	Lead Site	Other Participating Sites
				IRB approval	Open to accrual	Closed to accrual			
c06-012	A Randomized Phase II Study of Intermittent Chemotherapy or Intermittent Chemotherapy with Maintenance GM-CSF in Patients with Previously Untreated Metastatic HRPC	90	16/99	8/08	8/08	N/A	Higano	UCSF	Duke OHSU
c06-014	Phase II Study of Dasatinib (BMS-354825) for Androgen-Deprived Progressive Prostate Cancer	97	28/102	2/07	3/07	8/08	Yu	Wisconsin	JHU MSKCC And other outside sites
c07-015	A Phase I, Open-Label, Dose-Escalation Safety and Pharmacokinetic Study of MDV3100 in Patients with Castration-Resistant Prostate Cancer	Up to 186	23/140	4/07	7/07	2/09	Yu	MSKCC	MD Anderson OHSU Outside sites
c08-018	A Phase Ib/2 Study to Assess the Safety and Efficacy of AMG 102 in Combination with Mitoxantrone and Prednisone in Subjects with Previously Treated Castrate Resistant Prostate Cancer	135	5/142	10/08	11/08	10/09	Higano	UCSF	OHSU Outside Sites
C08-019	A Phase II Trial of Genomic Guided Therapy with Dasatinib or Nilutamide in Metastatic CRPC	60	19/57	10/09	10/09	4/11	Yu	Duke	OHSU, MDA, DFCC, UCSF

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			In-House PI	Lead Site	Other Participating Sites
				IRB approval	Open to accrual	Closed to accrual			
c08-002	Prospective Validation of A Microarray-Based Docetaxel Response Signature in Metastatic, Hormone Refractory Prostate Cancer	48	0/15	6/09	6/09	4/11	Higano	Duke	OHSU, UCSF
c09-047	An Open Label, Phase 2 Trial of Immunotherapy with Sipuleucel-T (Provenge®) as Neoadjuvant Treatment in Men with Localized Prostate Cancer	40	0/50	3/11	Pending	N/A	Higano	UCSF	Other outside sites
b09-002	A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate (CB7630) Plus Prednisone with Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy	1193	1/1192	4/09	4/09	6/09	Yu	MSKCC	OHSU, MDA, Other outside sites Global Trial
b09-003	AFFIRM: A Multinational Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy	1170	4/1170	12/09	12/09	12/10	Higano	MSKCC	OHSU / Other outside sites Global Study
b09-005	A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Abiraterone Acetate (CB7630) Plus Prednisone in Asymptomatic or Mildly Symptomatic Patients with Metastatic Castration-Resistant Prostate Cancer	1000	14/1000	6/09	6/09	4/10	Yu	MSKCC	Global Study

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			In-House PI	Lead Site	Other Participating Sites
				IRB approval	Open to accrual	Closed to accrual			
c09-030	A Randomized, Placebo-Controlled, Double-Blind, Phase 3 Study Evaluating the Clinical Benefit of Adding Custirsen to Docetaxel Retreatment/Prednisone as an Option for Second-line Therapy in Men with Castrate Resistant Prostate Cancer	292	0/2	09/10	N/A	N/A	Higano	OHSU	Global Study
c09-028	Phase II Trial of Exogenous Testosterone Plue Dutasteride for Treatment of Castrate Metastatic Prostate Cancer	24	0/6	Canceled 12/10	N/A	12/10	Nelson	MSKCC	
c09-039	A Phase II Open Label, Single Arm Trial Evaluating KX2-391 in Patients with Bone Metastatic Castration-Resistant Prostate Cancer who have not Received Chemotherapy	47	4/31	4/10	5/10	N/A	Yu	JHU	Wisc, UofC, WSU
c09-056	A Phase I/IIa Study of Safety and Efficacy of Alpharadin® with Docetaxel in Patients with Bone Mestastases from Castration-Resistant Prostate Cancer	66	0/7	pending	pending	N/A	Yu	MSKCC	DFCI, JHU, UCSF, UofC
b10-006	A Randomized Double-Blind Phase 3 Trial Comparing Docetaxel Combined with Dasatinib to Docetaxel Combined with Placebo in Castration-Resistant Prostate Cancer	1380	4/1380	10/09	11/09	1/11	Yu	MSKCC	Duke, UofC Global study
c10-070	A Phase II Study of BKM-120 in Men with Metastatic Castration Resistant Prostate Cancer BKM-120 Investigator initiated Protocol	66	0/0	pending	pending	N/A	Yu	Duke	OHSU

LOI #	Protocol Title (Phase, Intervention, Population)	Target Accrual	Current Accrual (UWash/ Other Sites)	Trial Activation Dates			In-House PI	Lead Site	Other Participating Sites
				IRB approval	Open to accrual	Closed to accrual			
c10-072	An Open-Label, Phase 1/2 Safety, Pharmacokinetic, and Proof-of-Concept Study of ARN-509 in Patients with Progressive Advanced Castration-Resistant Prostate Cancer	132	0/15	pending	pending	N/A	Higano	MSKCC	DFCI, OHSU, JHU,UCSF, UMich, Wisc,
c10-75	A Phase II study of MAOA inhibitor plus docetaxel in patients currently receiving and progressing on docetaxel therapy	20	0/2	pending	pending	N/A	Yu	OHSU	Other sites in Canada
c11-079	A Randomized Discontinuation Study of XL184 in Subjects with Advanced Solid Tumors	420	0/78	pending	pending	N/A	Higano	DFCI	MSKCC, UCSF, UMich, WSU,

Table E: Quarterly Patient Accrual by the University of Washington from 2/11/07 through 3/31/2011

Quarter	Total Accrual by Quarter	Total Minority Accrual by Quarter	Funding Year Minority Accrual Totals	Therapeutic Trials by Year		Biomarker Trials By Year	
				Total Accrual	Minority Accrual	Total Accrual	Minority Accrual
1st Quarter 2007	5*	1	**6**	63*	6	NA	NA
2nd Quarter 2007	8	1					
3rd Quarter 2007	15	0					
4th Quarter 2007	18	2					
1st Quarter 2008	17	2					
2nd Quarter 2008	21	2	**7**	61	7	5	0
3rd Quarter 2008	14	1					
4th Quarter 2008	11	3					
1st Quarter 2009	20	1					
2nd Quarter 2009	12	1	**3**	52	2	15	1
3rd Quarter 2009	21	0					
4th Quarter 2009	14	1					
1st Quarter 2010	20	1					
2nd Quarter 2010	**19**	**2**	**4**	**42**	**2**	**7**	**2**
3rd Quarter 2010	**15**	**0**					
4th Quarter 2010	**7**	**0**					
1st Quarter 2011	**8**	**2**					
Total Accrual	**245**	**20**	**20**	**218**	**18**	**27**	**3**

* 3 patients were actually accrued in 2 trials in Q4 '06 prior to our initiation date into the Consortium, but post award.