

AD _____

Award Number: W81XWH-08-1-0556

TITLE: Feasibility Study of a Novel Diet-Based Intervention for Prostate Cancer

PRINCIPAL INVESTIGATOR: J. Kellogg Parsons, M.D., MHS

CONTRACTING ORGANIZATION: University of California
La Jolla, CA 92093-0934

REPORT DATE: September 2011

TYPE OF REPORT: Annual Summary

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

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE			<i>Form Approved</i> <i>OMB No. 0704-0188</i>		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE September 2011		2. REPORT TYPE Annual Summary		3. DATES COVERED 1 September 2010 – 31 August 2011	
4. TITLE AND SUBTITLE Feasibility Study of a Novel Diet-Based Intervention for Prostate Cancer			5a. CONTRACT NUMBER		
			5b. GRANT NUMBER W81XWH-08-1-0556		
			5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) J. Kellogg Parsons, M.D., MHS E-Mail: k0parsons@mail.ucsd.edu			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California La Jolla, CA 92093-0934			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 Our goal is to develop a practical, diet-based intervention for prostate cancer. We have implemented a randomized clinical trial of a novel dietary intervention that utilizes a central, telephone-based counseling program to promote vegetable intake among prostate cancer patients who are being treated with active surveillance. As part of this trial, we are testing whether a gene fusion biomarker will predict disease progression in this patient population. During the third year of the funding period, I accomplished seven major tasks. First, I oversaw the opening of the study and the randomization of 28 patients. Second, I obtained IRB approval at the San Diego VA Hospital. Third, I responded to administrative review of the DoD human subjects protection documents. Fourth, I continued my participation in the Cancer and Leukemia Group B cooperative study group. Fifth, I guided the implementation of the study protocol through regular contact with CALGB personnel and collaborators at participating sites. Sixth, I obtained endorsement of the study from the leadership of the Southwest Oncology Group. Finally, I presented an abstract to the 2011 Innovative Minds in Prostate Cancer Today conference.					
15. SUBJECT TERMS prostate cancer, diet, watchful waiting, active surveillance					
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	13	19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
Introduction.....	1
Body.....	2
Key Research Accomplishments.....	4
Reportable Outcomes.....	5
Conclusion.....	6
References.....	7
Appendix.....	8

I. Introduction

Despite substantial advances in early detection and treatment, prostate cancer remains the most commonly diagnosed non-cutaneous cancer and the second leading cause of cancer death among U.S. men. The enormous scope of this public health problem calls for the development of innovative approaches to prostate cancer prevention, control, and treatment.

One potential novel approach is dietary modification. Epidemiological and pre-clinical studies suggest that alterations in nutritional intake may protect against prostate cancer initiation and progression. However, despite widespread public interest in this topic, there are very few clinical studies investigating the potential benefits of diet-based interventions for prostate cancer.

We have successfully developed and pilot tested a telephone-based dietary intervention for prostate cancer patients based on well-established principles of social cognitive theory.^{1,2} This relatively straightforward, low-cost intervention—which increases vegetable intake and decreases fat intake—is the first to utilize diet as a form of primary clinical therapy for prostate cancer. Due to its practicality, simplicity, and proven benefits to cardiovascular and overall health, this intervention would be widely applicable. Use in an active surveillance (“watchful waiting”) population may potentially spare thousands of patients each year from the considerable side effects of surgery and radiation.

We hypothesize that a vegetable-intensive diet will decrease disease progression and improve quality of life in men with prostate cancer. Our goal is to develop a practical, diet-based intervention for prostate cancer. We have implemented a randomized clinical trial of a novel dietary intervention that utilizes a central, telephone-based counseling program to promote vegetable intake among prostate cancer patients who are being treated with active surveillance. As part of this trial, we are testing whether a gene fusion biomarker will predict disease progression in a sub-group of patients.

II. Body

Progress to Date

During the second year of the funding period, I have made substantial progress in 6 specific areas.

1. Opening of the study and randomization of patients

The study opened to national accrual in March 2011. As of September 29, 2011, 28 patients had been randomized: 10 at UCSD and 18 at other sites.

2. IRB approval at the San Diego VA

On May 27, 2011, I secured IRB approval from the San Diego VA—the final administrative step required to open the study to accrual at the San Diego VA.

3. Response to administrative review of revised DoD human subjects protection documents

I submitted a written response to the administrative review of the revised DoD human subjects protection materials.

4. Continued participation in Cancer and Leukemia Group B (CALGB)

I have continued to participate extensively in CALGB and correspond with scientific collaborators through e-mail and conference calls. I have supplied serial updates to CALGB leadership regarding the status of the study.

5. Oversight of the study protocol

As Protocol Chair, I share the ultimate responsibility for the orderly and scientific conduct of all research activities associated with the trial. In this capacity, I have continued to meet and correspond with CALGB personnel and study collaborators on a regular basis. I have participated in regular teleconference meetings with study personnel, overseen the approval and implementation of protocol amendments, and routinely fielded questions from study coordinators at participating sites on such topics as patient eligibility and protocol design.

6. Publications

I presented a poster at the DoD IMPaCT conference in Orlando March 9-11, 2011 (**Reportable Outcomes**). The poster, entitled “The Men’s Eating and Living (MEAL) Study: A Randomized Trial of Diet to Alter Disease Progression in Prostate Cancer Patients on Active Surveillance,” was selected for press release, and I attended the press conference on March 10, 2011.

7. Endorsement for the study by the Southwest Oncology Group (SWOG) leadership

The Southwest Oncology Group (SWOG) is, like CALGB, a National Cancer Institute sponsored clinical trials cooperative group. SWOG coordinates hundreds of clinical trials sites nationwide. I presented the study to the SWOG urological trials leadership, who in turn issued an official endorsement of the study which should substantially increase the number of potential sites nationwide (**Appendix**).

Problem areas

There are no current problems impeding performance. The trial is now activated and accruing patients.

The original grant timeline estimated that the trial would open to accrual in March 2009. With the additional time required to secure funding and guide the CALGB protocol through the review processes, the trial is 24 months behind the original schedule. The timeline will require revision to account for this delay; however, the new timeline will depend in part as to how quickly the accrual goal of 464 patients is met.

Work to be performed during next reporting period

I have five goals for the next reporting period: 1) continue to accrue patients to study at the Moores UCSD Cancer Center; 2) begin to accrue patients to study at the San Diego VA; 3) continue oversight of the study protocol; and 4) continue planning of a new study timeline depending upon how quickly patients accrue to study.

III. Key Research Accomplishments

- Opened the study to accrual and randomization of patients
 - 28 patients randomized to study as of September 29, 2011
- Obtained IRB approval at the San Diego VA
- Responded to administrative review of DoD human subjects protection documents
- Participated in Cancer and Leukemia Group B (CALGB) activities
- Oversaw implementation of the study protocol
 - Corresponded with CALGB personnel and collaborators at participating sites
 - Approved and implemented several protocol amendments
 - Answered questions from study coordinators at participating sites
- Obtained endorsement for the study by the Southwest Oncology Group (SWOG) leadership
- Presented an abstract to the 2011 Innovative Minds in Prostate Cancer Today (IMPACT) Conference

IV. Reportable Outcomes

Abstracts

Parsons JK, Pierce JP, and Marshall J. The Men's Eating and Living (MEAL) Study: a randomized trial of diet to alter disease progression in prostate cancer patients on active surveillance. Submitted to Innovative Minds in Prostate Cancer Today Conference, Washington D.C., March 2011.

Background and objectives

There is widespread interest among physicians and patients in utilizing diet for the prevention and treatment of prostate cancer. Despite robust epidemiological and pre-clinical data suggesting that dietary modifications may alter prostate cancer initiation and progression, however, there remains a dearth of clinical trials. We will study the effect of a vegetable-intense diet on disease progression in prostate cancer patients on active surveillance.

Brief description of methodologies

The Men's Eating and Living (MEAL) study is a randomized, Phase III clinical trial designed to test the effect of diet intervention on disease progression in prostate cancer patients on active surveillance. This multicenter national trial is being run through Cancer and Leukemia Group B (CALGB) and the National Cancer Institute (NCI). The primary outcome is disease progression defined by total PSA, PSA doubling time, and pathology (Gleason sum and tumor volume) on repeat prostate biopsy. Participants are considered to have reached study endpoint if they progress by any one of these criteria. Secondary outcomes include treatment seeking, anxiety, and quality of life.

The diet intervention is a unique, validated, telephone-based communication and counseling system designed to promote vegetable intake in prostate cancer patients. We previously demonstrated the efficacy of this intervention for effecting diet change in a randomized clinical trial of 74 patients. An important nuance of diet intervention trials is that participants may be inclined to exaggerate their compliance with diet goals on questionnaires. Thus, we will measure serum carotenoid concentrations—an objective biomarker of vegetable intake—to independently verify diet composition.

In prior cohort studies of active surveillance patients, 2-year progression varied from 20% to 35%. Using the log-rank test with a two-sided $\alpha = 5\%$, a sample size of 418 will provide 80% power to detect a difference in progression rate (PGR) of 20% in the control and 10% in the experimental arm during 24 months of follow-up. Under the exponential distributions for the time to progression, the 2-year PGR of 20% vs. 10% corresponds to a hazard ratio (HR) of 0.472. Assuming a 10% dropout rate (including patients who are treated before progression), a total of 464 patients will be enrolled to this trial.

Results to date

We hypothesize that our intervention will decrease disease progression, decrease the incidence of active treatment, diminish anxiety, and improve quality of life for prostate cancer patients on active surveillance.

Conclusions

The MEAL study is the first large, multi-center, randomized clinical trial of diet for the treatment of prostate cancer and the first major, federally funded study of an intervention targeted for active surveillance patients.

Impact statement describing the potential impact on research, patient care, or quality of life

The MEAL study uniquely and simultaneously addresses two understudied yet highly topical themes in the treatment of prostate cancer: active surveillance and dietary intervention. The synthesis of these two aims—optimizing management of active surveillance patients through diet—represents a novel approach with a high potential for providing near-term patient benefits that would serve not only the prostate cancer population, but also the broader public health.

V. Conclusion

In summary, I achieved substantial progress during the third year of the funding period. I oversaw the opening of the study, obtained IRB approval at the San Diego VA, responded to administrative review of the DoD human subjects protection documents, continued to participate in Cancer and Leukemia Group B (CALGB), oversaw amendments to the study protocol, corresponded with CALGB personnel and collaborators at participating sites, obtained endorsement of the study from the Southwest Oncology Group (SWOG) leadership, and presented an abstract at the 2011 Innovative Minds in Prostate Cancer Today (IMPACT) Conference.

VI. References

1. Parsons JK, Newman V, Mohler JL, Pierce JP, Flatt S, and Marshall J. Dietary modification in prostate cancer patients on active surveillance: a randomized, multi-center feasibility study. *BJU Int*, 101: 1227-1231, 2008.
2. Parsons JK, Newman V, Mohler J, Pierce JP, Paskett E, and Marshall J. The Men's Eating and Living (MEAL) Study: A Cancer and Leukemia Group B pilot trial of dietary intervention for the treatment of prostate cancer. *Urology*, 72: 633-7, 2008.

VII. Appendix

Letter of Endorsement from the Southwest Oncology Group (SWOG)



TO: CALGB Vice Chair Gini Fleming, MD May 23, 2011
CALGB Administrator Trinidad Ajazi
CALGB-70807 Protocol Team J. Kellogg Parsons, MD, MHS
James R. Marshall, PhD
John Pierce, PhD
Michelle Naughton, PhD
Cheryl L. Rock, PhD, RD
Peter Humphrey, MD
James Mohler, MD
Electra Paskett, PhD
Laura Archer, MS
Sin-Ho Jung, PhD
Nick Jeffries
James R. Marshall, PhD

CALGB Prevention Subcommittee
Chair James R. Marshall, PhD
CALGB-70807 Protocol
Coordinator Julia Melnick

CC: SWOG Chair Laurence Baker, DO
SWOG Administrator Nathan Eriksen
SWOG Prevention Committee
Chairs Powel H. Brown, MD, PhD
Gary E. Goodman, MD
New SWOG Co-Chair Peter Van Veldhuizen, Jr., MD
New SWOG Protocol Contact at
Operations Office Patricia O'Kane
CTSUSU Project Director Steve Riordan
CTSUSU Protocol Specialist Emily Demske
DCP Acting Director Lori Minasian, MD, FACP

FROM: CTSUSU Project Officer Mike Montello, PharmD

SUBJECT: CTSUSU Co-Chair Designation for CALGB-70807

The Southwest Oncology Group (SWOG) has elected to 'endorse' through the CTSUSU mechanism CALGB-70807, "The Men's Eating and Living (MEAL) Study: A Randomized Trial of Diet to Alter Disease Progression in Prostate Cancer Patients on Active Surveillance." Peter Van Veldhuizen, Jr., MD will be joining the CALGB-70807 protocol team as the SWOG Co-Chair. As agreed upon by the Cooperative Group Chairs, the Co-Chair from SWOG will have many of the same responsibilities and privileges as any study co-chair that was assigned via the traditional 'Intergroup' mechanism:

- The Co-Chair will report on the study (accrual status, amendments, toxicity update) at SWOG meetings and promote it actively within the Group.
- Per capita and federally-funded ancillary reimbursement for enrollments credited to the SWOG will be paid by SWOG, unless other arrangements have been made with the NCI.
- SWOG will be responsible for auditing patients whose enrollments are credited to SWOG.

- The Group Chair of the SWOG will make all decisions regarding the authorship rights of the designated co-chair(s).
- The SWOG confirms that the individual named as Co-Chair does not have any conflicts of interest, per the policy and procedures of the SWOG, for the study named above.

The Cancer and Leukemia Group B (CALGB) will be responsible for circulating all revisions of the protocol to Dr. Peter Van Veldhuizen, Jr. for feedback prior to CTEP submission. As the Lead Group for CALGB-70807, CALGB should actively collaborate with Dr. Peter Van Veldhuizen, Jr. and should include both the SWOG group name and Dr. Peter Van Veldhuizen, Jr.'s name on the "face page" of the protocol, thereby formalizing the endorsement process. **The face page of the protocol should also clearly state the following: All Cooperative Group members who are not aligned with CALGB will enroll patients to this study via the Cancer Trials Support Unit (CTSU).** If the study is already active, this addition may be handled as a simple administrative amendment, for example:

The following Cooperative Groups have endorsed this trial:
SWOG: Co-chair Peter Van Veldhuizen, Jr., MD. **SWOG members will enroll patients to this study via the Cancer Trials Support Unit (CTSU).**

As with all protocols on the CTSU menu, the CTSU will provide administrative support to SWOG by performing the regulatory review and credentialing of SWOG's sites and investigators. A separate page is attached to this memorandum, identifying the contact information for Dr. Peter Van Veldhuizen, Jr. and Patricia O'Kane, the protocol contact at the SWOG's operations office.

If you have any questions about this process, please call me at 301-435-9206.

We hope that the addition of SWOG investigators to this CALGB-led study helps to boost accrual to this important trial. We would appreciate if the CALGB study leadership would now communicate directly with Dr. Peter Van Veldhuizen, Jr. to update him on any issues regarding the protocol and its conduct that you believe would help him to more knowledgeably promote and monitor the study within SWOG. Please let us know if we can be of any further assistance.