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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

This project is conducting a randomized double-blind clinical trial to assess the ability of a soy protein dietary supplement to reduce prostate cancer risk in older men. A total of 120 men (60 white and 60 African-American) aged 50 years or older with high PSA levels but normal prostate biopsies will be randomized into one of two groups (soy protein supplementation with isoflavones or casein protein supplementation). The specific aims are: 1) to determine the impact of the interventions, including changes in clinical (PSA levels and prostate volume) and intermediate (Ki-67, apoptosis, sex-steroid receptors, angiogenesis, antioxidant enzyme expression) markers of prostate cancer risk; 2) to assess soy protein effects on hormone levels, plasma lipids/lipoproteins and blood pressure; and 3) to evaluate changes in health-related quality of life, including urinary symptoms and sexual functioning. This project involves a multidisciplinary team affiliated with the oncology, Epidemiology, health-related quality of life, biostatistics, and nutrition. NCI approved of the CALGB protocol delayed start-up of this study; recruitment has been continuous since March 2000. However, recruitment to this study has been suspended per DOD Human Subjects Protection Office. Limited access status was changed to include all CALGB member institutions in recruitment on November 2001. Eight institutions have opened the protocol.

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INTRODUCTION

Soybeans and other legumes contain large amounts of plant estrogens know as isoflavones. Specific isoflavones found in soy (genistein and diadzein) have been implicated in reducing breast, colon, and prostate cancer risk in both laboratory-based studies [1]. Strong evidence for an effect on prostate cancer risk comes from cross-cultural studies, which have shown that prostate cancer rates are much lower in the Pacific Rim countries where soy products comprise a much higher proportion of the normal diet compared to the United States [2]. This study proposes to conduct a randomized double-blind clinical trial, which will assess the ability of a soy protein dietary supplement (a rich source of isoflavones) to reduce prostate cancer risk in older men. This project will randomize 120 men (60 white and 60 African-American) aged 55 years and older with high PSA levels but normal prostate biopsies into one of two groups (soy protein supplementation with isoflavones or casein protein supplementations). The specific aims are: 1) to determine the impact of the interventions, including changes in clinical (PSA levels and prostate volume) and intermediate (Ki-67, apoptosis, sex-steroid receptors, angiogenesis, antioxidant enzyme expression) markers of prostate cancer risk [3,4]; 2) to assess soy protein effects on hormone levels, plasma lipids/lipoproteins and blood pressure; and 3) to evaluate changes in health-related quality of life, including urinary symptoms and sexual functioning. This project will involve the collaborative efforts of a multidisciplinary team affiliated with the cooperative group, Cancer and Leukemia Group B (CALGB), which has substantial expertise in the areas of controlled clinical trials, oncology, epidemiology, health-related quality of life, biostatistics, and nutrition. If positive results are obtained in this trial, soy supplementation may provide an important tool for the prevention of prostate cancer.

BODY: Accomplishments associated with the approved statement of work.

Task 1:

a. Annual renewal of the consent, study forms and questionnaires that were developed and approved by the CALGB and NCI.
b. Wake Forest University School of Medicine (WFUSM) disseminated the soy and casein supplements received from PTI to the participating sites.
c. Staff training sessions continues to be held in conjunction with the annual meetings of the CALGB. All sites have not had the opportunity to attend; however staff have been identified and contacted at each of the remote sites. Training for the sites that did not attend the annual meetings will be done via phone.

Task 2:

a. Eight sites within CALGB have agreed to participate as of March 2003. Additional sites may open the study.
b. The recruitment phase has been slow due to the changes in the procedures to complete prostate biopsies. More biopsy specimens are being gathered during the biopsy procedure, thus more likely than not, if a biopsy is performed, the diagnosis is 90% positive for cancer, reducing our pool of potential participants.
c. Discussion and approval from the urology clinic physicians to begin the screening of their patients coming in for biopsies has been accomplished. However because of standing contracts (with pharmaceutical companies) many private urologists are pulling away from the low paying projects (such as ours) to use their patients for the higher income projects.

KEY RESEARCH ACCOMPLISHMENTS

Sites completed their individual Institutional Review Board approvals and began recruitment. Wake Forest University School of Medicine shipped product to all sites. Samples obtained to this point are being batched at Ralston for test to be run collectively. We have also secured arrangements with MD Anderson to use a Food Frequency questionnaire with added soy-containing foods for this study. We have opened the study to the whole membership of the CALGB as an answer to the slow recruitment numbers. We have recruited 8 sites. Dr. Paskett moved to Ohio State University in January, 2002. WFUSM transferred the contract to OSU. IRB approval was sought and obtained from OSU IRB. We are awaiting approval from the DOD Human Subjects Protection Office. This process has been ongoing for the past 14 months. In the meantime we have had to suspend recruitment activities until the pending issues with the DOD Human Subjects Protection Office is being resolved. We anticipate finalizing this in the couple of weeks. We have obtained matching funds from OSU (as WFUSM was originally to provide) to conduct this study.

REPORTABLE OUTCOMES

None to report during this annual reporting period.

CONCLUSION

Although this should be the final report, we have requested and received a no cost extension of this study. As previously reported, first our protocol was delayed over 14 months at the NCI. Then we had to wait longer for CALGB approval, activation, and institutional (various sites) IRB approvals. Task 2 has been slowed dramatically due to the current prostate biopsy guidelines; more of the biopsies that are being performed because of elevated PSA test results are positive. This has reduced the number of eligible men for the study. With the opening of the study to all CALGB sites, we should have better recruitment. Dr. Paskett's move to OSU and transferring the grant caused more delays. In addition, recruitment activities have to be suspended per DOD Human Subjects Protection Office. This is due to the Dr. Paskett's transfer from WFUSM to OSU and the addition of the other CALGB clinical centers participating in this project. Please note that risks to subjects have not changed and all sites participating through CALGB has received approval from their local IRBs.

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