RACIAL DIFFERENCES IN PROSTATE CANCER: INFLUENCE OF HEALTH CARE INTERACTION AND HOST AND TUMOR BIOLOGY

PUBLIC ABSTRACT

James L. Mohler, M.D., Consortium Director

Background Prostate cancer is the most common cancer in men and the second leading cause of cancer mortality. In men younger than 65 years of age, the prostate cancer mortality rate for African Americans is 3.1 times that of Caucasian Americans. In men 65 years of age and older, the prostate cancer mortality rate for African Americans is 2.3 times that of Caucasian Americans. Three potential reasons have been suggested frequently to explain the disproportionate mortality from prostate cancer in African Americans compared to Caucasian Americans. First, African Americans present more often with advanced, incurable prostate cancer because of more limited access to health care due to socioeconomic status resulting in decreased participation in early detection programs. Second, once diagnosed with potentially curable prostate cancer, effective treatments are chosen less often by African Americans; for example, African Americans have been reported more likely to observe prostate cancer. Finally, prostate cancer is biologically more aggressive in African Americans than Caucasian Americans. Among men treated by radical prostatectomy, race alone was found prognostically important when age, Gleason grade and clinical stage were controlled in multivariate analysis.

Hypothesis The mortality rate from prostate cancer is more than two-fold higher in African Americans compared to Caucasian Americans due to racial differences in 1) interaction with the health care system, 2) diet and biology of the host and/or 3) characteristics of the tumor.

Proposal Investigators from the University of North Carolina, Roswell Park Cancer Institute, Louisiana State University, Wake Forest University, Duke University Medical Center, Harvard University, Johns Hopkins Medical Center, Boston University, University of California at Irvine, University of South Carolina, National Institute for Environmental Health Sciences, and George Mason University have joined together to address critical aims in a large cohort of patients with newly-diagnosed prostate cancer. Two thousand patients, 1000 from North Carolina of whom 500 are African American and 500 are Caucasian, and 1000 from Louisiana of whom 500 are African American and 500 are Caucasian, will be identified by rapid case ascertainment and undergo in-home interview and blood, urine, toenail, and adipose tissue sampling. Slides of tissue sections will be produced to define biochemical parameters of prostate cancer aggressiveness, and tissue microarrays will be constructed from prostate tissue specimens obtained for research subjects selecting prostatectomy. The proposal will be able to address directly racial differences in prostate cancer mortality since African Americans in North Carolina have one of the highest, and African Americans in Louisiana have one of the lowest mortality rates from prostate cancer in the United States. Caucasian Americans in the two states have similar prostate cancer mortality that is less than either African American group.

Reasons for the disparity in prostate cancer outcome by race will be tested on three levels. First, African Americans may present with more advanced prostate cancer due to delay in diagnosis. Racial differences in interaction with the health care system will be evaluated by examining early detection behavior; socioeconomic status; attitudes, beliefs and knowledge; health care access; patient-physician communication; patient decision-making; alternative treatment use; and treatment choices.

Second, the races may have biological differences that impact prostate cancer aggressiveness due to their genetic composition or their behavior (diet and environment). Racial differences will be sought in diet with an emphasis upon antioxidant and fat consumption; levels of testosterone in the blood; exposure to carcinogens; expression of prostate cancer susceptibility genes such as genes in the

androgen metabolism pathway; genes that detoxify carcinogens and repair DNA damage; genes responsible for hereditary prostate cancer; and blood protein profiles associated with CaP aggressiveness.

Last, prostate cancer may be more aggressive in African Americans because of racial differences in tumor characteristics. Racial differences will be examined in tumor extent (clinical stage and serum PSA, a surrogate for tumor volume), tumor differentiation (Gleason grade) and tumor growth rate (calculated from tumor apoptosis and cell proliferation rates); expression of androgen receptor, androgen receptor co-activators and androgen-regulated genes; and stem-like cells (from which the most aggressive cancers may originate).

End Products Two major products will result from the proposed studies. First, an invaluable resource of clinical data (demographic; tumor stage and grade), serum, adipose tissue, and slides and microarrays of prostate cancer tissue will be available for further studies and, over time, outcome studies from 2000 men with newly diagnosed prostate cancer of whom 1000 are African American. Second, a comprehensive and coordinated characterization of racial differences in interaction with the health care system, host biology and tumor characteristics will be conducted in a large study cohort from two geographic areas chosen to maximize the likelihood of discerning racial differences important in disparate prostate cancer outcome. These studies will demonstrate whether public health resources should be focused upon altering critical patient-health care system interaction or altering patient or tumor biology to reduce prostate cancer mortality, in general, and prostate cancer mortality in African Americans, specifically.