Prostate Cancer Screening: Is Human Carcinoma Antigen a more Valid Screening Test than Prostate-Specific Antigen?

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A. Study Purpose and Rationale

Prostate cancer is the second leading cause of mortality for men in the U.S. According to the American Cancer Society, an estimated 220,900 cases will be diagnosed in 2003 with approximately 30,200 deaths due to prostate cancer. The natural history of prostate cancer is highly variable, ranging from indolent disease to aggressive cell lines. At the risk of over-treating men with prostate cancer, current screening practices are aimed at early detection. The American Urological Association currently recommends prostate cancer screening for all men over the age of 50, African American men over the age of 40 and men older than 40 who have a positive family history. Screening involves a prostate-specific antigen (PSA) level and a digital rectal exam (DRE). Approximately 75% of men in the U.S. older than 50 have been screened for prostate cancer using PSA (Punglia et al., 2003). The advantages of PSA are its reproducibility, its non-invasive nature, it is relatively inexpensive and it has greater sensitivity and specificity compared to DRE (Carroll et al, 2001). The disadvantages of PSA are that it is not specific to prostate cancer and it varies with age, race and prostate volume. The determination of a universal sensitivity and specificity of PSA is impossible given such dependence on multiple variables. A review of the literature demonstrates cited sensitivities for PSA ranging from 35% to 74% and specificity ranging from 39% to 88%. While PSA has been instrumental in the increased detection of prostate cancer, clearly there is a need for another screening test with improved predictive power.

Human carcinoma antigen (HCA) has been linked to epithelial derived cancers, such as prostate cancer, and is currently being studied by Egenix, Inc. Although little data has been published regarding HCA, a study aimed at identifying metastatic breast cancer patients reported a sensitivity of 93% and a specificity of 90%. In light of such data, HCA holds promise as screening test for prostate cancer.

B. Study Design and Procedure

This is a single-center, cross sectional study. Enrolled patients will undergo screening for prostate cancer, including both a serum PSA level and a HCA level. Patients who have a PSA level <4.0ng/mL and a negative HCA will undergo no further intervention and will continue to have the option of annual PSA screening. Patients who have either a PSA level >4.0ng/mL or a positive HCA will undergo prostate biopsy, even if both screening tests do not indicate biopsy. While Egenix, Inc. will perform the HCA assay, the PSA levels and the indicated biopsies will be performed at CPMC. HCA collection kits will be provided to all study recruiters. Using sensitivity and specificity of 60% and 75% for PSA and a projected sensitivity and specificity of 80% and 90% for HCA, 56 patients will be needed to complete the study.

a. Outcomes and Statistical Analysis

The data will be pooled from all participating subjects and used to determine both the sensitivity and specificity of the HCA assay. Chi-square analysis will be used to determine the significance of the validity of HCA in comparison to the validity of PSA for an alpha of 0.05 and a power of 80%.

C. Subject Selection and Recruitment

Faculty in the Department of Urology at CPMC will identify potential subjects. In order to ensure adequate enrollment of minority patients, recruitment will be extended to the department's affiliates at the Allen Pavilion and at Harlem Hospital. The identifying physician will obtain informed

consent and ensure that each patient has made an independent decision to undergo prostate cancer screening after appropriate counseling.

a. *Inclusion Criteria*: men ≥60 years old, consent to undergo prostate biopsy for either a PSA >4.0ng/mL or a positive HCA

b. *Exclusion Criteria*: diagnosis of prostate cancer, past or present use of finasteride, diagnosis of prostatitis, prostate biopsy or transurethral resection of the prostate within three months

D. Confidentiality of Study Data

Unique identification numbers will replace all personal identifiers. Only the principal investigator and the study coordinator will have all access to complete patient information. Under no circumstances will Egenix, Inc. have access to PSA levels and biopsy results until all data is collected and ready for analysis.

E. Potential Conflicts of Interest

None. No compensation in any form will be provided to participating physicians.

F. Potential Risks and Benefits

The risks involved in collection of serum for PSA and HCA are negligible. Prostate biopsy, if indicated by screening results, involves a minimal risk of bleeding and infection. Such risks will be outlined with patients before informed consent is obtained. Potential benefits include the opportunity to aid in the development of a novel method for prostate cancer screening.

G. Compensation

No compensation will be awarded. Subjects will not have to pay for the HCA assay.

H. References

Carroll *et al*. Prostate-Specific Antigen Best Practice Policy- Part I: Early Detection and Diagnosis of Prostate Cancer. *Urology*. 2001;57:217-224.

Codington *et al*. Immunologic quantification of the carcinoma specific human carcinoma antigen in clinical samples. *Cancer.* 2002;94:803-813.

Gann *et al.* A Prospective Evaluation of Plasma Prostate-Specific Antigen for Detection of Prostate Cancer. *JAMA*. 1995;273(4):289-294.

Punglia *et al*. Effect of Verification Bias on Screening for Prostate Cancer by Prostate-Specific Antigen. *NEJM*. 2003;349(4):335-342.