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TITLE: Breast Cancer Biomarkers in Nipple Aspirates from Women Treated with Estrogen Receptor Blockers

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

The purpose of our study is to determine if 1) success in collecting nipple aspirate fluid (NAF) biomarkers increases with experience, 2) NAF biomarkers (cytology, ploidy, cell cycle parameters, and prostate-specific antigen, PSA) change in response to treatment with tamoxifen (TAM) or raloxifene (RAL), and 3) NAF biomarker changes are associated with future breast cancer risk. Our hypothesis is that NAF biomarkers will change favorably or unfavorably in response to treatment with TAM or RAL, and that the biomarker change(s) will predate clinical findings observed on mammography or physical examination. Postmenopausal women at increased breast cancer risk are enrolled in the Study of Tamoxifen and Raloxifene (STAR) trial and randomized to TAM or RAL. Prior to starting medication, subjects who elect to participate undergo breast nipple aspiration. A repeat aspiration is performed 6 months after initiating medication. This multiinstitutional trial currently involves three centers (Thomas Jefferson University, UCLA and Fox Chase Cancer Center). Enrollment to date is 11, and 7 subjects have completed the trial. Analysis of the data has not yet been performed. A fourth site, MD Anderson Cancer Center, is currently considering joining the study. If our hypothesis proves correct, then nipple aspiration may provide a useful noninvasive method to evaluate response to treatment.

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INTRODUCTION

We are enrolling postmenopausal women at increased breast cancer risk who have entered the Study of Tamoxifen and Raloxifene (STAR) trial. Our study collects nipple aspirate fluid (NAF) prior to starting and 6 months after initiating tamoxifen (TAM) or raloxifene (RAL), as called for by the STAR trial. The purpose of our study is to determine if 1) success in collecting nipple aspirate fluid (NAF) increases with experience, 2) NAF biomarkers (cytology, ploidy, cell cycle parameters, and prostate-specific antigen, PSA) change in response to treatment with TAM or RAL, and 3) NAF biomarker changes are associated with future breast cancer risk. Our hypothesis is that NAF biomarkers will respond to treatment with TAM or RAL, and that the biomarker change(s) will predate clinical findings observed on mammography or physical examination. This multiinstitutional trial currently involves three centers (Thomas Jefferson University, UCLA and Fox Chase Cancer Center). If our hypothesis proves correct, then nipple aspiration may provide a useful noninvasive method to evaluate response to treatment.

BODY

Below we address each task in the approved Statement of Work.

Task 1. Evaluate the success of dedicated individuals in performing nipple aspiration (Months 1-32).

A. Notify physicians at Thomas Jefferson University and its Network Hospitals, as well as at the University of California at Los Angeles (UCLA) and its participating institutions, that the study has begun (Months 1-3).

This has been done. We have also brought a third institution, Fox Chase Cancer Center, in to the study.

B. Dr. Sauter to UCLA to insure consistency among institutions in the nipple aspiration technique.

UCLA hired a nurse experienced in nipple aspiration whom I observed in 1999. There has been 100% success in collecting NAF at each institution thus far.

C. Enroll subjects for initial (Months 1-28) and repeat aspirations (Months 7-34).

This is ongoing.

D. Work with the data management programmers to establish data entry files for use by participating research laboratories (Months 1-6).

This has been done.

E. Evaluate the success of collecting nipple aspirate fluid during years 1, 2, and 3 (Months 24-36).

This task will occur later.

Task 2. Assess biomarkers obtained in samples

A. Begin evaluation of NAF specimens. Evaluate NAF cytology, ploidy, cell cycle parameters, and PSA (Months 1-32).

We have done this. Our sample size is insufficient for statistical analysis.

B. Finalize the analysis of specimens. Compare results in baseline vs treated samples.

This will be performed later.

C. Prepare an outline of NAF biomarkers which indicates how frequently and in which direction (favorable or unfavorable) each changed after treatment.

This will be done when our sample size is larger.

D. For each biomarker, determine if there is an association between a biomarker change after treatment with tamoxifen/raloxifene and risk of precancer/cancer in the breast. This determination will be made in Month 36 of the study and after all subjects have received 5 years of treatment.

This will be done later.

KEY RESEARCH ACCOMPLISHMENTS

- Preliminary evidence that nipple aspiration can be successfully taught and performed by health care providers at multiple institutions
- Recruitment of subjects at increased breast cancer risk enrolled on the STAR trial at multiple institutions with limited funding
- NAF sample analysis performed by experts at multiple instituions

REPORTABLE OUTCOMES

1. IRB approval at Thomas Jefferson University, UCLA and Fox Chase Cancer Center
2. 11 subjects enrolled, 7 have completed the trial
3. evaluation of all biomarkers for 8 of 11 samples thus far received
4. successful NAF collection from all sites for all subject visits

CONCLUSIONS

Our preliminary findings demonstrate that nipple aspiration can be learned and successfully performed at multiple institutions, indicating that it is feasible to perform the procedure on a wide scale, should useful biomarkers be identified.

REFERENCES

N/A

APPENDICES

N/A