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TITLE: Changes in Ovarian Stromal Function and Associated Symptoms in Premenopausal Women Undergoing Chemotherapy for Breast Cancer

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14. ABSTRACT The objective of this pilot study is to identify if androgen levels are adversely affected by adjuvant chemotherapy for breast cancer and whether low androgen levels are correlated with the frequency and severity of fatigue, weight gain, psychological symptoms, vasomotor symptoms and libido. A longitudinal, descriptive design will be used with questionnaires completed and blood drawn from 20 premenopausal women at 4 time periods: baseline (before treatment), mid-treatment, immediate post-treatment and 6 months later. Questionnaires include the Female Sexual Function Index, Greene Climacteric Scale, Profile of Mood States, Schwartz Fatigue Scale and a menses diary. Data analysis will involve descriptive statistics and plots of hormone levels over time as well as t-tests to examine changes in hormone levels. Correlational analysis will be done to look at the relationship of symptoms to hormone levels. We have currently enrolled 20 eligible women, 18 who have completed all study components. If a connection between low levels of androgens and symptoms is found, androgen replacement may be a viable treatment option for breast cancer survivors.					
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Statement of Work

Introduction

This annual report will provide an update on the progress made with the Department of Defense on the protocol “Changes in Ovarian Stromal Function and Associated Symptoms in Premenopausal women Undergoing Chemotherapy for Breast Cancer”. Final HSRRB and IRB approval was received 4/05 and recruitment began 6/1/05. The study is continuing under a no-cost extension (year one approved April 2005; year two approved June, 2006; year 3 approved July, 2007). To date we have 20 women enrolled in the pilot with 18 of whom have completed all study components. The remaining 2 women continue to be enrolled and have one remaining data point to complete.

Task 1: Work with a collaborative team to develop protocol of pilot study “Changes in Ovarian Stromal Function in Premenopausal Women Receiving Chemotherapy for Breast Cancer” months 1 and 2

Task completed with HSRRB and IRB approval received 4/05.

Task 2: Attend mentoring sessions and educational meetings, months 2 through 24.

Task completed prior to 2006 and 2007 no-cost extensions. I continue participation in several educational meetings and mentoring opportunities. My participation this past year includes:

- Work with Dr. Lynn Hartmann and her research team on her Center of Excellence in Breast Cancer grant. I have attend weekly meetings; participated in writing of articles, grant proposals and reports. I continue to work closely with the team of study coordinators and statistical team in the collection, clean-up and analysis of data as well as in management of the budget.
- Attended several educational meetings:
 - Monthly Oncology Nursing Society Meetings
 - Monthly Medical Oncology Society Meetings
 - Advanced NVivo class to build skills on using qualitative analysis package
- Work with Dr. Wes Petersen to use Nvivo for the analysis of qualitative data from a study exploring the perceived educational needs of women newly diagnosed with breast cancer.

Task 3: Get approval for pilot study, set up systems to implement study, months 3 - 6

The timeline for the study was delayed. Initial Mayo Clinic IRB approval was obtained November 26, 2002. DOD IRB revisions were made and subsequently approved by Mayo Clinic IRB on 7/29/2003 and 7/6/2004. Responses to recommendations/considerations put forth by the HSRRB minutes of September 22, 2004 were approved by the DOD March 17, 2005 and subsequently by Mayo Clinic IRB March 2005. With the short interval between final approval and the original research end date of July 31, 2005 and the award expiration date of August 31, 2005, a no-cost study extension was submitted and approval was granted April, 2005. The number of qualified patients were such that accrual was not reached by the end of the first no-cost study extension. With the desire to complete study accrual, a second no-cost study extension was submitted. The second approval was granted June, 2006. Follow-up of these women continues for 6 months after the initiation of chemotherapy. At the end of the second no-cost study extension, 20 women were enrolled in the study. Two of these women still need to

complete their 6 month follow-up. For this reason, a third no-cost extension was submitted. This no-cost extension was approved July, 2007. This extension will be used to complete follow-up of the two remaining women. In the case of drop-out of either of these women, they will be replaced.

Task 4: Accrue to study, months 7 - 18

Accrual began June 1, 2005. Initial accrual difficulty resulted from eligible women deciding to have chemotherapy at their home institution. We were able to work with our laboratory to facilitate the patient blood draws at their home institution and mailed back to Mayo Clinic. However, this approach also proved difficult due to processing and shipping of the blood. Our next approach was to collaborate with Mayo Clinic Jacksonville to enroll patients. We have enrolled all 20 women. Eighteen of these women have completed all 4 data points. Two women still need to complete the 6 month data collection.

Thirteen women eligible for this study refused participation. Three enrolled women had oophorectomies prior to study completion. One additional enrolled woman had a luteinizing hormone-releasing hormone agonist. We sought and obtained approval from Mayo and DOD IRBs to recruit additional women to account for these women becoming ineligible due to surgical/medical interventions (n = 4) that interfere with our outcome measures.

Task 5: Data entry and analysis, months 19-24.

Data has been entered into a database as it is received. We are currently conducting data error checks and data clean-up. Preliminary analyses of data will then be completed.

Task 6: Final analysis and report writing, month 24

Data collection is still underway.

Task 7: Strategize follow-up study and program of research based on pilot data, month 24.

Data collection is still underway.

Key Accomplishments

- Addressed pre-review considerations included in the HSRRB minutes of September 22, 2004
- Approval by HSRRB March 17, 2005, pending completion of paperwork by Mayo's Institutional Official
- Approval of changes for HSRRB minutes of September 22, 2004 by Mayo Clinic IRB March, 2005
- Approval of a one year no-cost extension April 2005 (to extend research period to July 31, 2006)
- Study opened for accrual June 1, 2005
- Approval of a second one year no-cost extension June 2006 (to extend research period to July 31, 2007)

- Accrual of 20 eligible women; 18 completed all data points and 2 have one data point remaining as of August 1, 2007
- Approval of a third one year no-cost extension July 2006 (to extend research period to July 31, 2008)

Reportable Outcomes

- Reviewed manuscripts for *JAMA and Archives, Journal of Clinical Oncology, Cancer, Psycho-Oncology* as a means to enhance my knowledge regarding critical writing skills and publications.
- Attended a two day Nvivo class to learn this qualitative software package; attended a second advanced Nvivo class to increase skills using this software package.
- Publications in conjunction with

Dr. Lynn Hartmann and colleagues

- **Frost MH**, Slezak JM, Tran NV, Williams CI, Johnson JL, Woods JE, Petty PM, Donohue JH, Grant CS, Sloan JA, Sellers TA, Hartmann LC. Satisfaction after contralateral prophylactic mastectomy: The significance of mastectomy type, reconstructive complications, and body appearance. *Journal of Clinical Oncology*. 2005;23(31):7849-56.
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Conclusions

I have continued to have the opportunity to work with several researchers and their teams as a means to build my knowledge in regards to quality of life research, statistical procedures, team approaches to research, the article review process, manuscript preparation and submission, grant preparation and grant reports.

We have enrolled the proposed 20 eligible women for this pilot study. Eighteen of these women have completed all four data points. Two women have only their six month data point remaining. We are in the process of data clean-up and conducting preliminary analyses. Final data analysis will occur when all data has been collected.