

AD _____

Award Number: DAMD17-99-1-9428

TITLE: Apoptosis Based Gene Therapy of Breast Cancer

PRINCIPAL INVESTIGATOR: Stephen E. Karp, M.D.

CONTRACTING ORGANIZATION: Lahey Clinic
Burlington, Massachusetts 01805

REPORT DATE: August 2004

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE August 2004	3. REPORT TYPE AND DATES COVERED Annual Summary (1 Aug 2003 - 31 Jul 2004)	
4. TITLE AND SUBTITLE Apoptosis Based Gene Therapy of Breast Cancer			5. FUNDING NUMBERS DAMD17-99-1-9428	
6. AUTHOR(S) Stephen E. Karp, M.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Lahey Clinic Burlington, Massachusetts 01805 <i>E-Mail:</i> Stephen.e.karp@lahey.org			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) The focus of this project is to improve the clinical research efforts of the Lahey Clinic in breast cancer. The Clinic provides care to over 200 women / year with newly diagnosed breast cancer. The primary goal of this project is to increase the number of women at the Lahey Clinic who participate in clinical studies that evaluate new diagnostic techniques and treatments for women with breast cancer. Unfortunately we did not reach our objective of 20 patients as stated in our statement of work. The major factor was that trial closure limited opportunities for patient enrolment. We have been successful in participating in diagnostic studies for breast cancer, accruing 500 patients this year to studies evaluating new imaging techniques for breast cancer. I developed a prospective process for identification and accrual of new breast cancer patients. I, as well, developed a system that enhances accrual by initiating a formal evaluation process for new breast cancer protocols being considered by our clinicians. We evaluate protocols for scientific merit, feasibility based upon expected patient population size, and economic factors. We believe this committee will help promote patient accrual to breast cancer trials. We hope these efforts will augment clinical trial participation.				
14. SUBJECT TERMS Breast cancer clinical trials			15. NUMBER OF PAGES 6	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)

20050705 036

Table of Contents

Cover	1
SF 298	2
Table of Contents	3
Introduction	4
Body	4-6
Key Research Accomplishments	6
Reportable Outcomes	6
Conclusions	6
References	6
Appendices	6

Introduction

The focus of this research project is to improve the clinical research efforts of the Lahey Clinic in breast cancer. The Clinic provides breast cancer care to over 200 women / year with newly diagnosed breast cancer. The primary goal of this project is to increase the number of women at the Lahey Clinic who participate in clinical studies that evaluate new diagnostic techniques and treatments for women with breast cancer. We intend to improve accrual to these studies by opening new studies in breast cancer and to increase accrual to existing studies by increasing awareness of current studies and systematically assessing eligibility for our open studies for all women with newly diagnosed breast cancer. Moreover the project aims to increase accrual to such studies by systematically evaluating all newly diagnosed patients with breast cancer for eligibility in one of our studies.

Body

Task 1: Increase Participation in Breast Cancer Clinical Trials

For the grant year August 2003 – August 2004 we entered 13 patients onto breast cancer treatment and prevention studies. The study population and accrual numbers are listed in Table 1.

Table: Accrual to Breast Cancer Treatment Studies 2003- 2004

Study Name	Population	Number Enrolled	Comments
CALGB 49801	Low grade DCIS	2	
CALGB 40101	Node Negative Breast Cancer	1	
NSABP B30	Node Positive Breast Cancer	0	Closed on 3/31/04
NSABP B33	Aromatase Inhibitor after Tamoxifen	0	Closed on 10/0/03
NSABP B34	Node Negative Breast Cancer	1	Closed on 3/31/04
NSABP B35	Antiestrogen Therapy for DCIS	2	
NSABP P2	Antiestrogen Chemoprevention of Breast Cancer	7	
SOFT	Ovarian Suppression in Premenopausal Breast Cancer	0	
CA163046	Epothilone in Metastatic Breast Cancer	0	

Unfortunately we did not reach our objective of 20 patients as stated in our statement of work. There are two principal reasons why this occurred. The first factor was that trial closure limited opportunities for patient enrolment. Our preoperative chemotherapy trial NSABP B27 had closed and its replacement trial still has not opened. Thus we are unable to enroll patients with locally advanced or large primary breast tumors. Our node positive protocol B30 closed during the year and was not replaced until October 2004. Accrual to B30 prior to its closure was hurt by the publication of the benefits of dose dense chemotherapy. Many patients refused randomization to B30 because of the shorter duration of off protocol dose dense therapy. Accrual to node negative trials was influenced by the closure of B34, and by refusal of patients to participate in CAGB 40101, which potentially randomized favorable prognosis node negative patients to taxane chemotherapy. Enrollment in DCIS studies continues and is improving. The prevention study, P2 accrued well, but is now closed.

A second factor in poor accrual has been the resignation of two of our six medical oncologists over this year. The remaining ones, feeling overburdened have been reluctant to treat patients on study. Two new oncologists have been hired and will start February 2005. Nonetheless we can do better with accrual and will strive to do so this year.

We have as well opened two new studies for the diagnosis of breast cancer. The first study is an industrial collaboration that evaluates HEDA, Homologous Electrical Difference Analysis, a form of impedance technology, as an alternative to mammography for breast cancer diagnosis. This study: A Multicenter Clinical Study to Determine the Effectiveness and Safety of HEDA in the Screening of Women for Breast Cancer, opened in November 2003 and accrued 268 patients by August 2004. We have opened a second study of HEDA in patients undergoing stereotactic breast biopsy in November 2004.

We as well participated in the ACRIN DMIST study evaluating digital mammography. This study opened at our center in 2002 and we added a further 232 patients from August 2003 - August 2004. It closed to new patient accrual in 2004.

Task 2: Create a Centralized Data Management Structure

In order to enhance participation in clinical trials I have collaborated with the Lahey Clinic Research Department to prospectively identify all newly diagnosed patients with breast cancer and to evaluate them for trial participation. The pathology department identifies all new diagnoses of breast cancer by CPT code, (i.e. codes 233 and 174), and informs the research office. Research personal review the clinical information, determines eligibility, and informs the treating physician that the patient is a protocol candidate. At the next patient visit, a reminder is placed on the chart, as well as, a form that asks whether the patient entered onto study, and if not, why not. We have tracked all newly diagnosed breast cancer to date. Formal analysis of this data is underway. However, preliminary evaluation suggests that patient ineligibility or patient refusal is the major barriers to wider accrual.

Task 3: Create Clinical Trial Model

In order to create a system that enhances accrual we have developed a formal evaluation process for new breast cancer, and other, protocols being considered by our clinicians. In previous years clinicians were able to open any trial they desired, and often few patients were accrued with little focus or direction. To concentrate our efforts I developed a Cancer Trial committee, which reports to the hospital cancer committee. This committee sets priorities and evaluates and determines which trials may go forward to the Institutional Review Board for approval. This committee, which I chair, meets biweekly and consists of clinicians from the various cancer disciplines as well as members of the research office. We evaluate protocols for scientific merit, feasibility based upon expected patient population size, and economic factors. We believe this committee will help promote patient accrual to breast cancer trials.

Key Research Accomplishments

- Accrued 11 patients to Breast Cancer Treatment Trials
- Accrued 500 patients to Breast Cancer Diagnosis Studies
- Developed prospective process for identification and accrual of new breast cancer patients
- Developed Cancer Trial Committee for new trial evaluation and selection

Reportable Outcomes

None at present

Conclusions

We have endeavored to increase participation in clinical treatment trials of women with breast cancer at our institution. Our goal was to double accrual to 20 patients / year. We were not successful in this, accruing only 13 patients this year. Reasons for this include closure of several of our trials, and physician reluctance to participate secondary to manpower shortages. We have replaced those physicians lost. We have developed formal structures to better select clinical trials to participate in, and to enhance accrual to those studies we have opened.

We have been successful in participating in diagnostic studies for breast cancer, accruing 500 patients this year to studies evaluating new imaging techniques for breast cancer. We will continue to promote this effort in the future.

References

None

Appendices

None