Seeds4Hope

A program of the Windsor Essex County Cancer Centre Foundation

2010 Seeds4Hope Grant Recipient

Dr. Caroline Hamm

"Correlation of Spy-1 levels in patients during a phase II trial of patients with triple negative breast cancer receiving carboplatin with dose dense adriamycin /cyclophosphamide/taxol in combination with carboplatin"

SUMMARY OF RESEARCH PROJECT

Approximately one in ten women is diagnosed with breast cancer. Of these women, one in nine will have a unique type of breast cancer, now being called "triple negative" breast cancer (TNBC). It is called triple negative because the three targets we use for therapy are lacking on the cancer. The three targets are the estrogen receptor, the progesterone receptor and Her-2-neu, the target of herceptin. Since the cancer is lacking these targets, the only way we can prevent cancer recurrence in these women is chemotherapy. Women with this type of cancer tend to be younger and present with a higher stage of cancer. Because of this, they tend to have a higher risk of cancer recurrence and death from their cancer.

There is increasing evidence in the literature that this TNBC group of women will benefit from the addition of a fourth type of chemotherapy to their chemotherapy regimen, carboplatin. We are proposing a study that adds carboplatin to one of our current standard of care chemotherapies. We have already treated a small number of women with this protocol, using informed consent, and these women have had excellent tolerance of this regimen, and in very short follow-up, have done well without recurrence.

We plan to treat ninety triple negative breast cancer patients with this chemotherapy and measure improvement in disease control at five years. This will be in comparison to women with TNBC that we have treated at the Windsor Regional Cancer Centre before we started this protocol.

In addition to this chemotherapy change, we are testing the cancer for a new type of protein that research demonstrates may play a role in the development of this particular tumor type, Spy-1. We will determine whether this protein could be a valuable target for treatment and/or in guiding the physicians decisions with regard to treatment options. Furthermore, this work will determine whether Spy-1 levels will correlate with tumor type and with poor response to therapy, and will help us develop a novel target for treatment in the future.

HOW THIS RESEARCH HELPS ADVANCE QUALITY CANCER CARE IN OUR COMMUNITY

Women with 'triple negative breast cancer', represent a younger patient population being, on average, 11 years younger than women that do not have this type of cancer. Furthermore, they are 15% more likely to die from their cancer. This work will determine if this altered chemotherapy protocol will change this later statistic. In preliminary testing, women have tolerated this treatment very well, and in the few women we have treated to date, they continue to do well.

We are also very excited to bring this trial to a new level by adding in a diagnostic component to evaluate the prevalence of a promising biomarker, Spy1. To do this testing of the patient tumor samples will occur in the laboratory with Dr. Porter at the University of Windsor, a highly recognized researcher. We have coordinated many clinical departments of Windsor Regional Hospital, and all have agreed to participate. The physicians in the radiology and pathology departments, in addition to the oncology and clinical trials departments will all work together to allow this translational component of this trial to be successful. This additional objective could reveal a novel biomarker for patient diagnosis/prognosis and potentially a future target for treatment in women with triple negative breast cancer.

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PROGRESS REPORT

1A. Objective 1: *Identify the incidence and strength of Spy-1 expression with the diagnosis of breast cancer; to determine if there has been a difference between the expression of Spy-1 between patients with triple negative breast cancer (TNBC) and those with non-TNBC. We also plan to study the correlation of Spy1 expression and the patient's response to chemotherapy.*

In Dr. Porter's lab, she has collected many actual human breast cancer control tissues in collaboration with Dr. Shum, Chief of Pathology, Pathology labs of Windsor Regional Hospital and Hotel Dieu Grace Hospital. She has begun tissue microarray with these controls. The triple negative blocks have been held longer by the clinical trials/ pathology department for a minimum of time necessary to ensure that patients will further information will not be necessary for clinical decision making. In the Porter lab, we are optimizing a new antibody for the Spy-1 molecule. This has been an ongoing project for the last year, primarily for cost-saving reasons. However, we plan to send out to get the affinity purification done if we do not achieve success in the near future. Materials for the control TMA's are complete. We are now able to use a new TMA scanner which was recently funded through a CFI. This will give us excellent quantification of these results.

1A. Objective 2: *To assess progression free and overall survival of triple negative breast cancer patients treated with a novel combination of chemotherapy: Dose Dense ACT plus carboplatin, in patients with the diagnosis of triple negative breast cancer.*

We have been very pleased with our accrual to this clinical trial to date. We are now entering our third year of the trial, and have accrued almost 1/3 of the necessary population. Unfortunately, it has taken us quite a while to open the trial at other centres. London has passed the trial through the Breast Cancer Group, and the clinicians there are quite interested in opening this trial. At this time, they are submitting it to their Clinical Trials financial assessment group. We expect this will pass. London has two and a half times the patient population we have, and we are confident that as they come on line with us, we will be able to complete the accrual. We are currently conversing with Sudbury as well. They are currently treating a patient with our protocol "off trial" as the patient was not willing to travel to Windsor, and the clinician at that centre was willing to move ahead with this protocol.

In addition is it encouraging, from a clinician standpoint, that CALGB (a large multicentre oncology group from the USA) has just opened an almost identical clinical trial for their triple negative group. Certainly they are also doing tissue micro-arrays, but ours will be unique with the addition of Spy-1.

1A. Objective 3: *To assess the hematologic and neurological toxicity of patients treated with chemotherapy regimen consisting of a standard of care, dose dense ACT, plus a fourth chemotherapy: carboplatin in patients with the diagnosis of triple negative breast cancer.*

We are not able to review all of the toxicity data as the clinical trial is running. However, we have had no serious adverse events reported in the clinical trial. In addition, we are establishing a Data Safety Monitoring Committee (DSMC) that will be necessary as we move into a multi-centre trial.