Public Abstract

Project Title: Tumor targeting of an immune super-activator in male and female metastatic breast cancer

Rationale: There is an increasing understanding that males and females can respond differently to various drugs. Recently, the National Institutes of Health has required researchers to justify if they don’t consider males and females equally in proposed studies. Unfortunately however, the argument that breast cancer is predominantly a female disease has allowed most breast cancer research to still be done solely in females. But of course, men do get breast cancer and there is very limited understanding of whether the disease behaves similarly in men and women. Currently, men are given the same treatments as women. One area of particular interest for metastatic breast cancer is the advent of immunotherapies. Treatments that are based on harnessing the power of a patient’s own immune system to seek and destroy cancer cells, wherever they are in the body, have generated a lot of hope for the future. There are different types of immunotherapy with checkpoint inhibitors being the best known. Checkpoint inhibitors work to stop anti-tumor immune cells being turned off. So far, we have learned that not all patients benefit from checkpoint inhibitors, and the specific impact of sex is not understood. However, it is known that cells of the immune system are differentially active in males and females, even in people with no disease. A new immunotherapy drug that we propose to test has a different mechanism than checkpoint inhibitors. This new drug works to turn on (or activate) anti-tumor immune cells. We don’t know yet how well it might work in breast cancer. Therefore, we have two related questions to ask in this study: (1) within breast cancer tissue, are immune cells differentially present or active in samples from men versus women?; and (2) using 2 mouse models of metastatic breast cancer, do males and females respond similarly to a novel immunotherapy drug and is this novel immunotherapy effective against metastatic breast cancer?

Goal: To test whether a new targeted immune activating agent is effective against male and female metastatic breast cancer using mouse models, and to profile the immune landscape in male and female breast cancer tissue samples.

Interim outcomes: The research proposed here is early phase. This means that positive results would still need additional studies before findings could impact patients directly. Outcome 1 – If we see an apparent difference in number, type and/or activation levels of immune cells in samples from male and female patients, it would suggest that future immunotherapy tests should be based around the type of immune cells present in men versus women. Since male breast cancers occur much less frequently than female breast cancers, there are fewer patient samples to do immune profiling in. We hope that this study would open the door to large collaborations so that a more diverse range of samples could be compared. Outcome 2 - In the drug study we are proposing to use two different models of breast cancer, which represent different metastatic breast cancer subtypes. Positive results from these mouse studies would be a first step towards doing the necessary safety studies before real clinical trials could be done in people.

Significance: Successful completion of these studies (a) would identify a novel immunotherapy approach that can perhaps provide hope for patients that do not benefit from checkpoint inhibitors; (b) would assess whether male and female metastatic breast cancers have similar immune profiles; and (c) would determine if male and female metastatic breast cancer responds similarly to an immune-modifying agent, which is currently unknown. Any one of these three outcomes has the potential to affect how patients – female or male – are treated in the future.