Play for P.I.N.K. Aquidneck Club Award 2021 Grantee Summary

Seeking to improve quality of life for patients with HER2-positive breast cancer

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BCRF INVESTIGATOR SINCE
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RESEARCH LANDSCAPE:

HER2 is an oncogene that plays a role in the development and progression of about 30 percent of breast cancers. Non-metastatic HER2-positive breast cancer, once lethal, is curable in more than 90 percent of cases, but the treatments can cause severe side effects. Current "one-size-fits-all" strategies treat all stage II and III HER2-positive breast cancer patients with multiple additional chemotherapy drugs after surgery, even though there is not a clear benefit to more chemotherapy. The excellent long-term outcomes of most patients treated with modern regimens for non-metastatic HER2-positive disease mean that now, patients who can be treated just as effectively with less toxic, less intensive therapy must be thoughtfully identified. Characteristics of a tumor include not only the stage, subtype, and molecular composition of the cancer, but also the state of the patient's immune system and the cancer's response to prior therapy. The future of breast cancer care is in considering all these factors to create an individualized treatment for each patient.

PROJECT IMPACT:

Dr. Winer's work is based on earlier studies showing that additional chemotherapies after surgery can have both short-term adverse effects such as nausea, fatigue, and hair loss as well as long-term effects including the potential of heart damage or secondary leukemia. Though chemotherapy-associated toxicities are common, they are still useful or necessary for patients with more aggressive cancers who can benefit from them. Dr. Winer aims to de-escalate the amount of chemotherapy while maintaining treatment efficacy, which will improve quality of life and decrease the chance of rare but serious chemotherapy complications.

Dr. Winer completed the DAPHNe clinical trial to examine less intensive chemotherapy regimens for 100 HER2-positive breast cancer patients who have excellent prognoses. Patients with stage II and III HER2-positive breast cancer were treated before surgery with the chemotherapy paclitaxel along with trastuzumab and pertuzumab (THP), two HER2-targeted antibody therapies. At the time of surgery, patients who did not have cancer in the breast or lymph nodes received further HER2-targeted medicines after surgery without any additional chemotherapy. The DAPHNe trial showed the feasibility and promise of this approach. The team has also begun analyzing tumor biopsies and blood samples collected during the DAPHNe trial, which will build knowledge of how a patient's immune system works with anti-HER2 antibody therapies to fight HER2-positive breast cancer. Dr. Winer has begun a follow-up clinical trial (MARGOT), the first large national trial incorporating the novel anti-HER2 antibody drug margetuximab into pre-operative treatment for HER2-positive breast cancer.

FUTURE PLANS AND GOALS:

Two large, prospective clinical trials are ongoing or planned to evaluate long-term outcomes associated with de-escalation in patients who achieve a pathologic complete response: CompassHER2-pCR and DECRESCENDO trials in the United States and Europe, respectively. Dr. Winer is also conducting two smaller phase II trials to explore feasibility and response rates of neoadjuvant THP or paclitaxel/margetuximab/pertuzumab (TMP) for stage II-III HER2-positive breast cancer. Dr. Winer will analyze biospecimen data from both trials with the overarching goal of better understanding the relationship between anti-HER2 antibody therapy, anti-tumor immune system mechanisms, and patients' clinical outcomes after neoadjuvant therapy.

In addition, Dr. Winer and his team will use data from these two trials along with three other recent Dana-Farber led trials to examine response rates to neoadjuvant HER2-directed therapy based on the variability of hormone receptor (HR) status and compare the immune microenvironment across HER2-positive tumors with varying degrees of HR expression. If de-escalation becomes an increasingly standard approach in the management of early-stage HER2-positive breast cancer, a better understanding of the differences between HER2-positive breast cancer that is HR-positive versus HR-negative is essential. By better understanding the relationship between treatment response and the variability in HR status, clinicians will be better equipped to design future treatment regimens.

INVESTIGATOR BIO:

Eric P. Winer, MD is a Professor of Medicine at Harvard Medical School, and Chief of Women's Cancers and Director of the Breast Oncology Program and the Thompson Chair in Breast Cancer Research at Dana-Farber Cancer Institute. He is the Principal Investigator of the Dana-Farber/Harvard Cancer Center SPORE in Breast Cancer, and he serves as the co-chair of the NCI Breast Cancer Steering Committee that oversees the breast cancer clinical trials sponsored by the National Cancer Institute. The Dana-Farber breast cancer program cares for thousands of individuals with breast cancer each year and has an extensive research portfolio with the goal of extending the lives of individuals with breast cancer and minimizing suffering from the disease. Dr. Winer has received numerous awards for breast cancer research and has also been recognized for his mentoring efforts. Broadly, his research focuses on improving the clinical care of women with breast cancer. He collaborates closely with colleagues in basic science, translational medicine, biostatistics, health services research, clinical oncology, and psychosocial research. Dr. Winer is a graduate of Yale College, with a degree in History and Russian/East European Studies. He subsequently obtained his medical degree from Yale School of Medicine, followed by training in internal medicine at Yale. He completed a fellowship in medical oncology at Duke University Medical Center and remained on the Duke Faculty until 1997, when he moved to Dana-Farber Cancer Institute in Boston to assume the role of Director of the Breast Oncology Center.