

Breast Cancer Moon Shot

Each year, approximately 270,000 patients in the U.S. face a breast cancer diagnosis. Although survival rates are steadily increasing, thanks in large part to improved diagnostics and targeted therapies, subsets of patients with forms of aggressive or resistant breast cancer are often left with a poor prognosis. Physicians and researchers at The University of Texas MD Anderson Cancer Center are working to improve the outlook for patients who have a notorious form of the disease, known as triple-negative breast cancer (TNBC), as part of the Breast Cancer Moon Shot®.

MD Anderson's Moon Shots Program® seeks to dramatically and quickly reduce the mortality of more than a dozen cancers — and eventually apply its unique research model to defeating all forms of cancer. Leaders of the Breast Cancer Moon Shot — Junjie Chen, Ph.D., chair of Experimental Radiation Oncology; Gaiane Rauch, M.D., Ph.D., professor of Abdominal Imaging; and Clinton Yam, M.D., assistant professor of Breast Medical Oncology — have set an ambitious scientific agenda that is executed by a talented, diverse and dedicated team of physicians, translational researchers and basic scientists.

About TNBC

Breast cancer is labeled TNBC when estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) expression are all absent. It accounts for between 15-20% of breast cancer cases and is associated with a younger age at diagnosis. But rather than being a singular form of cancer, TNBC is really a “catch all” term that encompasses many different molecular phenotypes. Many successful therapies for breast cancer are aimed at receptors absent in TNBC, so this subset of patients is often left looking for other clinical answers when standard chemotherapy fails them. Unfortunately, approximately half of TNBC tumors are resistant to chemotherapy or gradually develop a resistance. Triple-negative cancer cells are also more likely to spread to other areas of the body, making surgery alone less likely to lead to long-term absence of the cancer.

Personalization of therapy using a neoadjuvant approach

The Moon Shot® team is working to establish a precision medicine framework that will provide more effective, personalized treatment options for patients with localized TNBC. The goal of this project is to advance new treatments for those with chemo-insensitive disease while also preventing overtreatment of patients who respond well to chemotherapy. The cornerstone of this project is the ARTEMIS trial.

All patients enrolled in ARTEMIS start on standard chemotherapy. Researchers collect a tumor biopsy before and during treatment to evaluate clinical response. Patients who respond well continue their course of treatment leading up to surgery. Those who do not respond are then shifted to a targeted therapy trial based on characteristics of their tumor. Samples collected from patients not only inform the shaping of their personal treatment plans, but the data also provides a valuable resource to learn broadly about the disease and suggest novel therapeutic strategies.

Through analysis of these ARTEMIS samples, the research team identified several subtypes of TNBC based on gene expression signatures. These findings revealed signaling pathways that contribute to treatment resistance and could be treated with targeted therapies. MD Anderson has cultivated a portfolio of targeted therapy trials for patients with chemo-insensitive disease. The goal is to reliably recommend optimum therapies to match these gene signatures — meaning patients start and finish with the single best treatment option for their cancer.

For some patients with TNBC, complete response may be achievable with less therapy, including less chemotherapy or less targeted therapy as a first option. As one example, Moon Shot members led preliminary studies that resulted in a national trial evaluating the PARP inhibitor talazoparib as a single neoadjuvant therapy. When is it appropriate to de-escalate therapy — and spare patients from unnecessary toxicity, side effects and expense — while still preserving the efficacy of treatment? Work continues in this space, and additional studies are planned to better understand the right balances needed to serve such a diverse patient population.

Factors influencing a patient's immune response with TNBC

The tumor immune environment plays an important role in how patients with TNBC respond to neoadjuvant therapy, particularly with the presence tumor infiltrating lymphocytes (TIL) strongly associated with improved outcomes. This suggests that immunotherapy could be an incredibly beneficial treatment modality for breast cancer patients, but checkpoint inhibitors — which have offered tremendous benefits to patients with other types of cancer — have yet to yield the same effects in the breast cancer setting. The Moon Shot team is working to better understand why this is the case.

Researchers have begun to identify predictors of response to therapy for patients with only moderate TIL levels, including predictors like specific gene signatures and tumor markers. The team also is examining how immune response changes over the course of treatment by profiling biopsy samples taken before, during and after neoadjuvant therapy. This approach is uncovering new mechanisms of resistance for which clinicians can account for when designing treatment plans.



MD Anderson researchers have led the field exploring the role the microbiome plays in regulating response to therapy, and this includes projects within the Breast Cancer Moon Shot. Researchers are collecting samples of saliva and stool from patients with TNBC along the course of their treatment to correlate microbiome characteristics with response to various therapies. Evidence suggests that intestinal bacteria may play an important role how the immune system identifies tumor cells and modulates response to both chemotherapy and immunotherapy.

The impact of philanthropy

Private support for the Breast Cancer Moon Shot is critical to how quickly our team can find new and improved clinical answers for patients with TNBC. Funding for staff salary and research supplies is essential to keep the work moving forward. The bold and broad scope of projects already funded is possible because of MD Anderson's own investment in resources and thanks to many generous donors who believe in our ambitious vision. On behalf of all the patients and families affected by breast cancer here in Houston and around the world, please join us.

Together, we are truly Making Cancer History®.