MAYO CLINIC

BEAUTY AND PROMISE
Developing the New Gold Standard in Breast Care

Last year, over 40,000 women died from metastatic breast cancer in the United States. To address this health care need, Mayo Clinic's Center for Individualized Medicine created Project BEAUTY (to focus on early stage disease) and PROMISE (to focus on metastatic disease). Through these combined efforts, Mayo is transforming standards of care for people with breast cancer.

Project Background

The Breast Cancer Genome Guided Therapy Study (BEAUTY) aligned Mayo's multidisciplinary clinical breast cancer care services with our world-class researchers. The result was a prospective clinical trial where extensive DNA sequencing data was obtained before, during and after chemotherapy treatment for women with high-risk breast cancer. BEAUTY researchers preserved cancer cells from each woman enrolled in the BEAUTY study using a research technique known as patient derived xenografts, or PDX. New drugs were tested in the laboratory on these cancer cells, known to be either sensitive or resistant to conventional therapies. Mayo researchers used sequencing data, patient outcomes and xenografts to identify new cancer treatments. Based on these findings, Mayo initiated BEAUTY 2, a study in which new chemotherapy drugs are being prospectively tested in women with evidence for chemotherapy resistance.

Recent Progress

Through BEAUTY, in the past year Mayo researchers identified:

- A new drug target called CDK1, which is upregulated in ER+ tumors of women enrolled in BEAUTY (whose tumors were resistant to chemotherapy).
- A new drug that may be successful in targeting CDK1, researchers continue to investigate if this approach will help prevent resistance to chemotherapy.
- An aggressive subset of tumors (triple negative breast cancer) that also express a steroid hormone called the androgen receptor, this affects lower chemotherapy response rates than in women whose tumor did not express this receptor.
- A mutation in an important tumor suppressor gene (p53) that differed in women with the androgen receptor variant of triple negative breast cancer.

Mayo Clinic's Focus on Metastatic Breast Cancer

Mayo researchers now use the BEAUTY concept to focus on hormone receptor positive metastatic breast cancer. Hormone receptor positive (HRP) is the most common subtype of breast cancer. For many years our treatment approach was to "block" a patient's hormones with drugs like tamoxifen or ones that lower estrogen such as aromatase inhibitors. A new class of drugs called CDK 4/6 inhibitors has emerged as a gold standard. The first of its class to obtain Food and Drug Administration approval is palbociclib, two others (ribociclib and abemaciclib) are expected to also be approved.

Palbociclib helps block hormones and prevent breast cancer cells from developing resistance to hormone-based therapies. While this approach has been successful, (in a two-year span) nearly half of these women still undergo disease progression. Many of this group are treated with chemotherapy for a short period of time and succumb to their disease. For this reason, it is critical to understand the reasons why patients do or do not respond to CDK 4/6 inhibitors.

Mayo Clinic is building on the research success of BEAUTY by developing the new Prospective Study to Evaluate the Role of Sequencing in Women Receiving Palbociclib for Advanced Hormone Receptor (HR)-Positive Breast Cancer, or PROMISE. In PROMISE, women with hormone receptor positive metastatic breast cancer who intend to start treatment with the CDK 4/6 inhibitor palbociclib and hormone-based therapy will undergo tumor biopsies at baseline and at progression for sequencing. Patient-derived xenografts will also be generated from these biopsies to study properties of the original tumor.

By developing patient derived xenografts, Mayo researchers will be able to carefully study new drugs in the laboratory using the cancer cells that were derived from women that did and did not respond to palbociclib. The goal of this prospective study is to identify the molecular underpinnings of patient responses to CDK 4/6 inhibitors and change the way we care for people with metastatic breast cancer.

Philanthropic Need

There is a great medical need for new metastatic breast cancer treatment strategies. Benefactor gifts allow Mayo Clinic to accelerate metastatic breast cancer research through an individualized, comprehensive approach of tumor sequencing, patient derived xenografts and clinical care. This will allow Mayo experts to focus their efforts on obtaining critical information necessary to advance precise, personally-tailored therapies.