This guide is based on an expert panel discussion titled “Triple Negative Breast Cancer: Practical Treatment Strategies,” developed by the Triple Negative Breast Cancer Foundation and Medscape Education Oncology and supported by an independent educational grant from Eisai Pharmaceuticals.

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What is TNBC?

“All breast tumors that are not ER+, PR+ or HER2+ fall within the bucket of TNBC.”

— Eric P. Winer, MD

TNBC is a type of breast cancer that is defined by what it is not, rather than what it is. Today, all breast cancers are characterized using 3 biological factors: estrogen receptor (ER), progesterone receptor (PR), and HER2 expression status.

TNBC: Key Points

- Triple negative breast cancer (TNBC) is a subtype of breast cancer defined by the absence of the hormone receptors for estrogen and progesterone, as well as a lack of expression of a cancer-promoting protein known as HER2.

- TNBC occurs more frequently in women of color and is twice as common in black women as in white women in the United States.

- In the United States, about 15% of all breast cancers in white women are TNBC compared with 30% in black women. This means that on an annual basis, approximately 30,000 white women and 8200 black women will be diagnosed with TNBC.

- TNBC occurs more often in younger women and women with the BRCA1 mutation, a mutation in a gene that produces tumor-suppressor proteins.

- As with other breast cancer subtypes, mammography can be an effective means of detecting early stage TNBC.

- Early stage TNBC can be treated effectively with surgery, often followed by radiation and chemotherapy.

- Many patients with early stage TNBC are candidates for breast-conserving surgery.

- TNBC recurs more commonly than other types of breast cancer and accounts for a disproportionate percentage of breast cancer deaths. Recurrences almost always occur within the first 5 years after diagnosis.

- Adjuvant chemotherapy, which is treatment given after surgery for early breast cancer, can be highly effective for preventing disease recurrence.

- There are an increasing number of chemotherapy options for patients with advanced and recurrent TNBC. While these drugs are effective, responses tend to be short lived.

- There is an urgent need to develop targeted therapies to treat TNBC and an intense, focused effort is underway to achieve this goal.

- Genetic counseling is important for most patients with TNBC and their families.

This is important because these factors influence the treatment options that are available to women. Although hormone treatments and drugs that target HER2 expression are not effective for treating TNBC, it can be treated with surgery, radiation therapy, and chemotherapy.

As researchers understand more about the biology of breast cancer, they have identified several subtypes of TNBC. At this time, however, it is not clear how the determination of these subtypes might affect treatment selection and prognosis.
Who is at risk for TNBC?

“For unexplained reasons, women of African ancestry have a higher risk and incidence of TNBC.”
— Lisa A. Newman, MD, MPH

TNBC tends to occur more often in younger, premenopausal women and in women who have a BRCA1 mutation (although it is rare in women with a BRCA2 mutation). Since the BRCA1 mutation is more common in women of Ashkenazic Jewish descent, this group is at higher risk for TNBC.

Overall, TNBC accounts for about 20% of all breast cancers. This type of breast cancer occurs more frequently in women of African ancestry. In the United States, 30% of breast cancers in black women are triple negative. The reasons for this, according to Dr. Newman, are unknown. Hispanic women also have a higher incidence of TNBC compared with non-Hispanic white women.

Is it true that TNBC has a worse prognosis than other kinds of breast cancer?

“I would like to dispel the notion that some doctors and certainly many women with TNBC have, which is that everyone with TNBC does poorly. That is simply not the case.”
— Eric P. Winer, MD

When it is detected and diagnosed early and treated appropriately, the prognosis for women with TNBC is not significantly worse than it is for other types of breast cancer. That said, a woman diagnosed with TNBC is somewhat more likely to have a recurrence of disease than a woman with ER-positive or HER2-positive breast cancer. Women with recurrent TNBC are not eligible for the treatment options available to women with these other types of breast cancer. As a result, TNBC is responsible for a disproportionate number of breast cancer deaths.

TNBC also has a different pattern of disease recurrence than other types of breast cancer. A woman who has been successfully treated for TNBC and is disease-free 5 or more years has almost no risk of having the cancer come back. In addition, TNBC tends to spread to the lung and brain more often than to bone—-the most common site of metastasis for those with ER-positive breast cancer.

The risk for disease recurrence in women with TNBC is directly related to the size of the tumor and the number of positive lymph nodes found at the time of diagnosis. For women facing this disease it is important to know that early-stage TNBC is a highly treatable and often curable disease.

“I always tell my patients that no biological factor is going to turn a stage 1 breast cancer into a high-risk breast cancer.”
— Lisa A. Carey, MD

What is the role of genetic counseling for patients with TNBC?

“…This represents a nice opportunity to slow down the decision-making process about surgical options and think through all the information that is available, including genetic counseling.”
— Lisa A. Newman, MD, MPH

A diagnosis of TNBC carries with it the possibility of hereditary susceptibility, including the risk of carrying the BRCA1 genetic mutation. Currently, genetic counseling is recommended for every woman with a diagnosis of TNBC who is younger than age 60. This is even more important if the cancer is diagnosed at a young age, if the woman has a family history of breast cancer, or if she belongs to an ethnic or racial group with a known high risk. Genetic counseling will determine her BRCA1 mutation status, and also provide critically important information in helping to decide on treatment options. Should she, for example, consider prophylactic mastectomy and/or oophorectomy (removal of her ovaries)? Is she a candidate for breast-conserving surgery? What are the implications for other members of her family?
What is the role of neoadjuvant therapy in treating TNBC?

"For women with early stage TNBC, I would say, 'go ahead and have your surgery.' Let us see exactly what you have. Let us find out about your lymph node status, and then we will make decisions about adjuvant therapy."

— Eric P. Winer, MD

Adjuvant therapy is treatment given after surgery to reduce the risk for disease recurrence. In recent years there has been growing interest in using neoadjuvant therapy, which is chemotherapy given before surgery. The goal of neoadjuvant treatment is to achieve what is known as a pathologic complete response, which means that all visible signs of the breast cancer are gone before surgery. At this time, the role of neoadjuvant therapy in treating early TNBC remains unclear. Although some doctors advocate using neoadjuvant therapy for almost any woman with TNBC, this panel of experts generally supports having surgery first, evaluating the results, and then making the decision as to whether and what kind of adjuvant therapy might be appropriate.

For women with larger, more advanced tumors at the time of diagnosis, neoadjuvant therapy can be considered as a way to shrink or even eliminate the tumor prior to surgery and to improve the overall outcomes of treatment. However, according to Dr. Winer, the current data do not show that neoadjuvant therapy for women with TNBC increases the number of patients who become eligible for breast-conserving surgery.
What treatments are available for women with recurrent or metastatic TNBC?

“The first thing I usually think about when making a decision about chemotherapy for a woman with metastatic breast cancer is what kind of toxicity she is willing to accept.”

— Eric P. Winer, MD

If a woman is diagnosed with an advanced TNBC or her cancer recurs and spreads, there are a number of drugs that have been shown to be effective in controlling the disease. The decision about which of these drugs to use, whether to use them singly or in combination, and in what order to use them depends on a number of factors. These include the biology and history of the individual cancer, the doctor’s experience with the drugs, and the patient’s preference. Different drugs have different side effects. Platinum-based drugs, for example, do not cause hair loss, but may be associated with other substantial toxicities, such as nausea and vomiting, and kidney or nerve damage. And a newer chemotherapy drug, eribulin, has fewer gastrointestinal side effects than a standard oral agent, but may cause hair loss. It is important for every patient to have an honest conversation with her doctor about her goals and willingness to tolerate varying levels and types of treatment-related toxicity.

Most patients with advanced TNBC initially respond to one or more of the available drugs. The problem is that many of these responses are relatively short term. When the cancer becomes resistant to the drug, the disease begins to progress.

Patients with advanced TNBC should discuss with their doctors the possibility of participating in a clinical trial. There are currently a large number of trials underway designed to develop new treatments and improve outcomes with existing therapies. Cancer clinical trials usually offer standard therapy vs something new. Patients should not worry that they might receive placebo or might not be treated adequately as part of a study. The limited success of today’s treatments, however, makes this research about future therapies all the more urgent and underscores the importance of considering participation in appropriate trials.
Are there any targeted therapies for TNBC?

"What we all want is targeted therapy that can be applied broadly to a group (of patients with TNBC) that we can identify. That’s the Holy Grail. We haven’t found it yet, but we are getting there."

— Lisa A. Carey, MD

At this time, despite intense research efforts, there are no targeted therapies for TNBC.

"I think this is an evolving time in TNBC."

— Lisa A. Carey, MD

Future Directions for TNBC Research

Key research directions that may offer effective new therapies for TNBC in the near future include:

- Studying the role of poly ADP ribose polymerase (PARP) inhibitors, a new class of oral drugs that may be particularly effective for women with BRCA1-related tumors
- Understanding more about the biology of hereditary cancers, the BRCA-associated tumors, which may be particularly sensitive to treatment with platinum agents
- Tailoring chemotherapy according to individual patient and tumor variables
- Identifying targeted therapies that focus anti-cancer activity on a causative "target" rather than the entire body

"There are now more treatment options for TNBC and the prognosis has actually improved over time. The drugs we have are effective, so we are making advances. We are hopeful that that trajectory will continue."

— Lisa A. Carey, MD