Managing HER2-Positive Breast Cancer Amid COVID-19

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Breast cancer is the most commonly diagnosed cancer in U.S. women, and the second-leading cause of cancer-related deaths after the lung cancer. About 1 in 8 U.S. women (approximately 12%) will develop invasive breast cancer over the course of her lifetime. The average 5-year and 10-year survival rates in invasive non-metastatic breast cancer are 91 percent and 84 percent, respectively. The average 5-year survival rate is 86 percent when disease is spread to regional lymph nodes and 27 percent when it is metastasized to distant organs. These survival rates are 9 percent lower in African-American women overall.

The molecular characterization has significantly aided in the development of bringing clarity to “survivorship”

By Wendy S. Harpham, MD, FACP

When you see “Survivorship” in a headline, do you envision all your patients or only those who’ve completed therapy? Do you expect to read about medical interventions, quality-of-life issues, or advocacy? These days, any answers are reasonable—and that’s a problem.

As a physician-survivor I’ve grappled for decades with the ambiguity surrounding “survivorship.” Only recently did I see an urgent need to bring clarity to the term. Here’s my story, with a vision of how both clinicians and patients could benefit from universal adoption of a single, specific definition.

The word “survivorship” has troubled me since the first time I heard it in 1990, the week of my cancer diagnosis. Decades later, my discomfort grew when the term was adopted as shorthand for “post-treatment survivorship.” Like a vitreous floater, the annoyance wasn’t preventing me from writing about challenges in oncology care, so I kept working around it.

Then I read Judith Pearson’s From Shadows to Life—a Biography of the Cancer Survivorship Movement. Her stories took me back to an era before rainbow-colored rubber bracelets and digital communications, when patients...
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targeted therapies and improving overall survival rates. In this article, we will only focus on HER2-positive breast cancer. HER2 is amplified or overexpressed in about 15 percent of breast cancers. For patients with HER2-positive breast cancer, HER2-targeted therapy is recommended.

The choice of therapy for HER2-positive breast cancer is dependent upon the tumor size, nodal status, distant metastasis, and receptor subtype. The current treatment trend is focused on de-emphasizing anthracycline use, de-escalation of chemotherapy, increased monoclonal antibody use, and tailoring treatment based on response.


The addition of pertuzumab to trastuzumab was clinically superior in the neoadjuvant and adjuvant setting as demonstrated in NeoSphere and APHINITY trials (Lancet Oncol 2012;13(1):25-32; N Engl J Med 2017;377(2):122-31).

In the KATHERINE trial, the adjuvant use of T-DM1 for patients with residual disease in early HER-2 breast cancer after completion of neoadjuvant therapy demonstrated 50 percent less recurrence of invasive disease or death (N Engl J Med 2018;380(7):617-28). The use of weekly paclitaxel with trastuzumab (APT trial) and possibly adotrastuzumab emtansine (T-DM1) (ATEMPT trial) in stage I node-negative disease was as effective as more intense chemotherapy regimens (J Clin Oncol 2019;37(22):1868-75; ASCO Post 2020; Supplement: Conference Highlights SABCS 2019). Moreover, the addition of extended use of neratinib in the adjuvant setting may provide additional delay from recurrence in the appropriate patients (Lancet Oncol 2016;17(3):367-77).

Similar to the early setting, de-escalation has been the primary aim in metastatic disease, although chemotherapy remains an integral partner in the care of HER2-positive disease. Taxanes plus monoclonal antibodies, including pertuzumab and trastuzumab, have a solid foothold as first-line treatment. The antibody drug conjugate T-DM1 can also be used in first line in the appropriate population, and as a second line and beyond option.

Tucatinib, a select HER2 tyrosine kinase inhibitor combined with capcitabine and trastuzumab has shown progression-free and overall survival benefit, including in patients with CNS involvement, is an option for treatment in the second-line and beyond space.

The topoisomerase inhibitor conjugated to trastuzumab deruxtecan (T-DXd), or tyrosine kinase inhibitors neratinib or lapatinib, added to capcitabine if patients progress on initial trastuzumab regimen can be as third and beyond line of treatment. More recently margetuximab-cmkb, an Fc-engineered HER2 antibody combined with chemotherapy, was approved for third-line or greater metastatic HER2-positive breast cancers (JAMA Oncology 2021;7(4):573-84).

Breast Cancer & COVID-19

Although the patient experience has been an important factor in treatment development and selection for HER2-positive patients, this has been magnified in the setting of the SARS-CoV-2 (COVID-19) pandemic. The U.S. declared a national emergency shortly after the World Health Organization announced that COVID-19 had potential to become a global pandemic. This has significantly altered our way of life, particularly in the health care system. Patients diagnosed with breast cancer were no exception.

Initially, hospitals and clinics began cancelling or delaying diagnostic testing, elective surgeries, and other elective procedures to decrease the risk of exposure and save resources as COVID-19 cases surged, resulting in delays in care. Oncologists were forced to tailor care by triaging patients based on multiple factors, including current ECOG status, stage of disease, active treatment with chemotherapy or hormonal therapy, age, patients’ preference, other co-morbidities, and safety of staff and themselves.

The CDC and other oncology-related groups released guidelines to assist oncologists in managing their patients. However, given the numerous unknowns and the novelty of this virus, as well as the rapid pace of change, oncologists were bombarded with numerous updates and sometime conflicting management recommendations.

The CDC has included having cancer as an increased risk of developing serious complications due to a weakened immune system from chemotherapy or cancer itself contributed to uncertainty and a great source of anxiety for breast cancer patients and providers.

The medical community rapidly adapted to the changing situation and shifted care to virtual platforms. Oncologists tried to rearrange the logistics of their clinical practice and associated infusion center. Additionally, many clinicians redefined the chemotherapy protocols on a case-to-case basis. Some of these treatment alterations were meant to be permanent while others would revert once deemed safe.

Like many other oncology practices, the West Cancer Center and Research Institute (WCCRI) had to update its protocols to limit infection exposure and minimize physical contact. We initiated virtual patient visits, which dominated our patient interaction during the early stages, but has now been reduced to a handful of visits a day.

While this was initially difficult due to its novelty and rapid initiation, the WCCRI quickly accommodated to provide high-quality continuous care to our patients. Studies have indicated that telemedicine can be as effective as in-person visits. Moreover, studies in cancer population associate televisits with higher quality of life and less distress when compared with frequent physical visits (Ther Adv Chronic Dis 2020; doi: 10.1177/2040622320961597; J Telemed Telecare 2018; doi: 10.1177/1357633X16686777).

We initiated phone screening for COVID-19 symptoms with a brief questionnaire when patients arrive at an appointment. Additionally, temperature checks at the entry were mandated. In addition to social distancing, masks were to be worn by patients, staff, and providers while in the facility.

Although some institutions began testing all chemotherapy patients prior to treatment, at West we focused on the symptomatic, exposed, or COVID screen failure patients. Patients with COVID-19 positive tests were asked to delay the chemotherapy treatment and return following a 10- to 14-day quarantine and a negative test. Patients were also reassured that this may be important to protect them from developing the serious COVID-19 complications if they received chemotherapy while testing positive for the virus.

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Surgical procedures required a COVID-19 negative test beforehand. Other institutional changes included limiting the number of accompanying visitors to zero except for patients dependent on their caregiver. Laboratory-only visits scheduled prior to chemotherapy were sometimes offered at pop-up parking lot phlebotomy labs.

In addition to global institutional changes, COVID has impacted disease-specific management modifications. For example, in HER2-positive breast cancers, physicians gravitated toward less neutropenia-inducing regimens.

In the curative setting, there was an increase in utilization of weekly paclitaxel over docetaxel. Although less marrow suppressive, it required increased visits to the infusion center. For patients who were concerned about frequency of infusion visits, GM-CSF in the form of pegfilgrastim on-body injector was given with every docetaxel infusion without consideration to its companion drugs. This meant patients receiving every 3 weeks docetaxel with pertuzumab and trastuzumab also received pegfilgrastim support.

In some cases, the opposite occurred in that clinicians switched from weekly chemotherapy regimen to every 2-3 weeks regimen, which was selected based on clinician and patient preference where appropriate. For patients not appropriate for the APT regimen, we favored the use of the NeoSphere, which could allow 45 percent of patients receiving a pathologic complete response to exclude further chemotherapy. For patients who were candidates for the APT regimen, chemotherapy could be deferred for targeted anti-HER2 regimen based on the ATEMPT trial (Cancer Res 2020;80(4 Supplement):GS1-05-GS1). In that trial, T-DM1 offered similar disease-free survival at 3 years to weekly paclitaxel and trastuzumab.

In the metastatic setting, similar efforts to reduce the risk of neutropenia and reduce visits to the cancer center were made. If docetaxel was being utilized, then GM-CSF support was provided with it. In patients with persistent neutropenia secondary to advanced disease/chemotherapy treatment, antibody-only therapy was utilized. In some cases, we extended trastuzumab cycles to every 28 days dosing at 8 mg/kg. When possible, all oral regimens utilizing tyrosine kinase inhibitors (e.g., lapatinib, neratinib, and tucatinib) or anti-hormonal therapies with or without capecitabine were utilized. Antibody-drug conjugates with low neutropenic potential, such as T-DM1, were utilized when appropriate.

There is no doubt that the impact of the pandemic on cancer treatment and outcomes will be felt long after the virus reaches global equilibrium. Many clinical practice changes made during the pandemic, such as the incorporation of telehealth visits, are likely to become standard given their positive impact on cancer care. We must continue to evaluate the impact of regimen alterations both on patient satisfaction parameters and disease control going forward to allow for the best standard of care in this patient population. OT