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Treating Metastatic HER2-negative Breast Cancer

ONCOLOGY NURSING APPROACHES TO IMPROVE PATIENT QUALITY OF LIFE

ADVERSE EVENT **POCKET GUIDE PATIENT TOOL**

Adverse events (AEs) and side effects (SEs) are a major reason for treatment discontinuation and therapy nonadherence in patients with HER2-negative metastatic breast cancer (MBC). Clinicians and patients should consider which agents have the potential for treatment-related SEs and which therapy option is the most sustainable and likely to provide the best outcomes.

Once treatment has begun, it is important to remember that an experienced cancer care team is there to help you every step of the way. If you experience uncomfortable or unusual symptoms, it is important to call your care team while the symptom is “minor” rather than waiting for it to become more serious and potentially requiring emergency care that could lead to a pause in or discontinuation of therapy.

Treatment options for MBC include systemic chemotherapy and radiation therapy. There are benefits and limitations to each of these options, and their side effects should be considered prior to initiating therapy. As a patient, it is important that you understand what side-effects you may experience with different available treatment options before deciding on a treatment plan. You should know that your innate susceptibility to side effects is influenced by a number of factors, including your overall health and wellness level.

Antibody-Drug Conjugates

This guide provides information on a specific type of therapy: antibody-drug conjugates (ADCs). These agents are suitable for people with MBC who have already been treated with chemotherapy and another immunotherapy, and for people who are not able to have chemotherapy but have already received at least one other type of drug therapy.

ADCs work by delivering small doses of powerful chemotherapy into targeted cancerous cells. There are many combinations of antibodies and drugs, but so far, the only FDA-approved ADCs for MBC are sacituzumab govitecan (SG), datopotamab deruxtecan (Dato-DXd), and trastuzumab deruxtecan (T-DXd).

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Side Effects of Treatment with ADCs

Cancer treatments and cancer itself can affect your quality of life. Side effects occur when healthy tissues or organs are stressed. Talk to your care team regularly, and do not hesitate to tell them about any symptoms you may be experiencing. Other people receiving your treatment have very likely experienced the same side effects that you experience, and your health care team has strategies to reduce these side effects, so you will feel better. This table explains who is eligible to take the ADC options available for MBC; identifies common and/or potentially serious side effects of therapy; and discusses how ADCs are processed by the body and what can negatively impact effectiveness, absorption, or clearance of the toxic components of the therapy that cause side effects.

	Sacituzumab govitecan (SG)	**Datopotamab deruxtecan (Dato-DXd)**	**Trastuzumab deruxtecan (T-DXd)**
Indication	• Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) after two or more prior systemic therapies, at least one of them for metastatic disease • Unresectable locally advanced or metastatic hormone receptor positive (HR+)/HER2-neg (IHC 0, IHC 1+, or IHC 2+/ISH-neg) BC after endocrine-based therapy and at least two additional systemic therapies in the metastatic setting	• Unresectable or metastatic, HR+/HER2-neg (IHC 0, IHC 1+ or IHC 2+/ISH-) BC who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease	• Unresectable or metastatic HER2+ (IHC 3+ or ISH+) BC after a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy • Unresectable or metastatic HR+/HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) BC, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting • Unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-neg) BC, as determined by an FDA-approved test, after a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

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Common side effects

(these side effects presented in more than 10% of patients who participated in the pivotal trials for these therapies)

Sacituzumab govitecan (SG)	Datopotamab deruxtecan (Dato-DXd)	Trastuzumab deruxtecan (T-DXd)
• Fatigue • Diarrhea • Nausea/vomiting • Alopecia • Constipation • Abdominal pain • Decreased appetite • Stomatitis (sores in the mouth) • Cough • Fever • Urinary tract infection • Upper respiratory tract infection • Back pain • Generalized pain • Headache • Dizziness • Insomnia • Rash • Itching • Laboratory anomalies, including hyperglycemia, electrolyte imbalances, and liver dysfunction • Decreased hemoglobin, lymphocytes, neutrophils, and platelets	• Stomatitis • Nausea • Constipation • Vomiting • Diarrhea • Abdominal pain • Fatigue • Alopecia • Rash • Dry eye • Keratitis • Decreased appetite • COVID-19 • Cough • Laboratory anomalies, including electrolyte imbalances and liver dysfunction • Decreased hemoglobin, lymphocytes, and neutrophils	• Nausea • Vomiting • Fatigue • Alopecia • Constipation • Musculoskeletal pain • Diarrhea • Decreased appetite • Respiratory infection • Headache • Abdominal pain • Stomatitis • Decreased weight • Peripheral neuropathy • Dizziness • Dyspepsia • Epistaxis • Cough • Interstitial lung disease • Laboratory anomalies, including electrolyte imbalances and liver dysfunction • Decreased hemoglobin, lymphocytes, neutrophils, and platelets

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	Sacituzumab govitecan (SG)	Datopotamab deruxtecan (Dato-DXd)	Trastuzumab deruxtecan (T-DXd)
Serious side effects (these are side effects that, if not managed promptly, have the potential of causing significant harm)	• Febrile neutropenia—a reduction in the number of white blood cells occurring in association with a systemic infection—can be life threatening and occurred in about 6% of people, mostly within the first 3 weeks • Severe diarrhea resulted in dehydration in about 10% of people • Hypersensitivity and infusion-related reactions* are common, but severe responses occurred in fewer than 2% of patients • Nausea and vomiting may be severe in about 2% of people • SG can cause fetal harm	• Stomatitis (sores in the mouth and GI tract) occurred in 59% of patients with a median time to onset of 0.7 months • Although rare, severe, life-threatening or fatal pneumonitis/interstitial lung disease (ILD) can occur in approximately 4% of people and with an median time to onset of 3.5 months • Eye effects included dry eye, blurred vision, and conjunctivitis and were common (51%), with a median time to onset of 2.1 months • Dato-DXd can cause fetal harm	• Pneumonitis/ILD occurred in 12% of patients with a median time to onset of 5.5 months • Severe neutropenia, including febrile neutropenia, occurred in 65% of patients with a median time to onset of 3 weeks; febrile neutropenia was reported in ~1% of patients • Left ventricular ejection fraction (LVEF) decrease – a decrease in the heart's ability to pump blood and may preceed congestive hear failure – occurred in 4.6% of patients with 0.6% of patients developing severe LVEF decrease • T-DXd can cause fetal harm
Additional comments about ADC toxicity	The toxic part of SG (irinotecan) is metabolized by an enzyme called UGT1A1, which can affect the blood levels of irinotecan. This, in turn, can increase (or decrease) the incidence of side effects with SG use. Some people have a variant of the UGT1A1 enzyme that does not detoxify irinotecan as quickly, allowing the toxic part of SG to build up, which leads to a higher incidence of more severe adverse effects. Commercial tests are available for UGT1A1 polymorphisms.	Steroid mouthwashes and sucking on ice chips during infusion can reduce the incidence of stomatitis. Patients should immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms.	LVEF should be assessed prior to initiation of T-DXd and at regular intervals during treatment. Patients should immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms.

**A hypersensitivity reaction is like an allergic reaction, whereas an infusion-related reaction is an unexpected reaction that cannot be explained by an allergic reaction or the known toxicity profile of the drug.*

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ONCOLOGY NURSING APPROACHES TO IMPROVE PATIENT QUALITY OF LIFE

Cancer Fatigue

Cancer fatigue is one of the most common side effects of cancer treatment. The vast majority of people with cancer experience fatigue while receiving chemotherapy or radiation therapy. Fatigue can begin before, during, or after cancer treatment. Cancer itself, cancer treatments, and the side effects of treatment can cause fatigue. It is important that you try to rest and get good quality sleep. Support yourself with exercise, good nutrition, and mind-body practices. Try to plan your day around times that you are most likely to have less fatigue.

Diarrhea

Diarrhea can lead to dehydration and electrolyte imbalances and can be life threatening. Call your health care team if you feel dizzy or lightheaded, have dark yellow urine or are not urinating, or have a fever of 100.5°F (38°C) or higher. Drink plenty of fluids each day, preferably water. Try to eat frequent, small meals, and avoid foods and drinks that make diarrhea worse (e.g., caffeinated drinks).

Nausea and Vomiting

Nausea and vomiting are common side effects of cancer treatments, and if uncontrolled, vomiting can lead to dehydration, electrolyte imbalances, and weight loss. Nausea and vomiting resulting from chemotherapy may begin a few minutes to a few hours after treatment begins, or it may be delayed and occur a day or more after treatment. Nausea usually lasts 24–48 hours, but some people may feel sick for up to 7 days after treatment. Typically, patients are prescribed antinausea medicines before chemotherapy starts, because once nausea and vomiting from chemotherapy develop, they are more difficult to treat. Your doctor may prescribe multiple types of medicines called antiemetics that you can take to control nausea and vomiting, and will tell you when to take the antiemetics, such as before or after chemotherapy treatments or a certain amount of time before eating. It is also helpful to drink plenty of fluids and eat more frequent, smaller meals that are easy on your stomach.

Peripheral Neuropathy

Peripheral neuropathy is a result of damage to the peripheral nerves (nerves outside of the brain and spinal cord). Side effects depend on which peripheral nerves (sensory, motor, or autonomic [bodily functions]) are affected.

- Damage to sensory nerves may cause pins-and-needles sensations, pain, or numbness
- Damage to motor nerves may cause weak muscles and balance or fine motor control problems
- Damage to autonomic nerves may cause difficulty controlling blood pressure, digestion, heart rate, and/or body temperature

Treating Metastatic HER2-negative Breast Cancer

ONCOLOGY NURSING APPROACHES TO IMPROVE PATIENT QUALITY OF LIFE

Try to minimize trip hazards and change your physical surroundings to reduce the risk of falls. It is also important to remain vigilant in the kitchen and bathroom, protecting your hands and feet from heat, cold, and abrasions.

Stomatitis

Cancer treatments can cause painful sores in your mouth and throat that interfere with eating and drinking. If you have stomatitis, eating soft, wet foods or shakes and smoothies may be helpful.

Alopecia

Hair loss is very common and is one of the most distressing effects of chemotherapy. Scalp cooling (or cold caps) during therapy may help preserve some hair, but results vary. Being gentle with your hair (using a wide-tooth comb, and avoiding hair dryers or gel products) may also preserve some of your hair. Many people with hair loss choose to wear hats, scarves, turbans, or wraps. Wigs and hairpieces can also be used to help maintain or build confidence, self-esteem, and a sense of normalcy during cancer treatment; and many cancer centers and organizations provide access to or financial assistance for wigs for cancer patients. It is important that you protect your scalp and use sunscreen when not wearing a head covering. It may take 2–3 months after the end of chemotherapy for your hair to grow back.

When to Talk to Your Care Team

As a general point, if you experience new or worsening symptoms, call your care team to alert them of this. Less severe symptoms are usually easier to manage than more severe symptoms. Your care team may be able to offer an approach to make your symptoms more tolerable while maintaining therapeutic efficacy. Remember, you are not alone in your cancer journey. Your care team is there to help you manage side effects and point you to additional physical, psychological/emotional, and financial support services. They want to help you, so do not hesitate to talk to them.

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ONCOLOGY NURSING APPROACHES TO IMPROVE PATIENT QUALITY OF LIFE

Additional Resources

Many support groups are available to help patients cope with breast cancer. In addition to groups on Facebook, LinkedIn, Reddit, and other social media sites, these organizations can help you connect with other patients and resources.

National Breast Cancer Foundation, Inc.	nationalbreastcancer.org
American Cancer Society Cancer Survivors Network	csn.cancer.org
Cancer Support Community / Gilda's Club	cancersupportcommunity.org
AABCA African American Breast Cancer Alliance	aabcainc.org
METAVIVOR Metastatic Breast Cancer Research, Support and Awareness	metavivor.org
touch The Black Breast Cancer Alliance	touchbbca.org
CancerCare	cancercare.org
Susan G. Komen	www.komen.org
The Chrysalis Initiative	thechrysalisinitiative.org