TREATMENT UPDATE:

Gastric Cancer

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In recent years, new treatment approaches have been developed to treat gastric cancer.

Gastric cancer is relatively rare compared to other types of cancer, with about 26,000 new cases diagnosed in the United States annually. It mostly occurs in people over age 65 and is more common in men than in women. More than 95 percent of gastric cancers are adenocarcinomas, meaning they start from cells located in the glands of the stomach.

Stages of Gastric Cancer

The stages of adenocarcinomas and other forms of gastric cancer describe how far the cancer has spread at the time of diagnosis. The stage of the cancer will guide treatment options.

Stage 0

The cancer is limited to the mucosa (the innermost layer of the stomach wall).

Stage IA

The cancer has spread completely through the mucosa but has not spread to lymph nodes or the muscularis (the middle layer of the stomach wall).

Stage IB

The cancer has spread completely through the mucosa and has also spread to the muscularis or to six or fewer lymph nodes.

Stage II

The cancer has spread completely through the mucosa and is found in the muscularis and one or more lymph nodes, or is found in the wall of the serosa (outermost layer of the stomach) but is not found in lymph nodes or other organs.

Stage III

The cancer has spread completely through the muscularis and is found in the wall of the serosa and one or more lymph nodes.

Stage IV

The cancer is found in organs next to the stomach or in other parts of the body.

Metastatic Gastric Cancer

Metastatic gastric cancer is another term for stage IV gastric cancer. Cancer is said to have metastasized when it has spread to other areas of the body. These locations can include the liver, abdominal lining (peritoneum), lungs, brain and/or bones. Because the cancer cells in these other locations are identical to the gastric cancer cells, they are still considered gastric cancer rather than a separate form of cancer.

Treatment Options by Stage

Stages 0 and IA

Stages 0 and IA gastric cancers are best treated by minimally invasive endoscopic surgery, in which the doctor removes the tumor through an endoscope (lighted tube) that is inserted into the stomach through the mouth. Endoscopic surgery is best done by a gastroenterologist with experience in these complex procedures. Alternatively, a gastrectomy (surgical removal of part or all of the stomach) and lymphadenectomy (removal of the nearby lymph nodes) can be performed, but this is more invasive surgery and should be avoided if possible. Typically, no additional therapy beyond surgery is needed.

Stages IB, II and III

Stage IB, II or III gastric cancer is treated with a total or partial gastrectomy and lymphadenectomy. Chemotherapy may be given both before surgery to shrink the cancer and after surgery to destroy any remaining cancer cells. Chemotherapy may be given after surgery, especially if cancer cells are found in the removed lymph nodes. Chemoradiation (chemotherapy plus radiation therapy) may also be given after surgery, but that approach is becoming increasingly less common. People who are not able to undergo surgery are often treated with chemotherapy, radiation or chemoradiation.

Stage IV and Metastatic

Treatments for stage IV gastric cancer are designed to shrink the tumor and help relieve symptoms. The primary treatment approaches are chemotherapy, targeted therapy and immunotherapy. Surgery, radiation or chemoradiation may also be considered, but are less common.

Treatment Descriptions

Surgery

When surgery is part of the treatment plan for gastric cancer, the approach depends on the stage of the cancer and other factors unique to the individual.

Subtotal (partial) gastrectomy. In a subtotal gastrectomy, the cancerous portion of the stomach is removed. Most often, a subtotal gastrectomy is performed if the cancer is in the lower portion of the stomach (near the intestines), although it may sometimes be performed if the cancer is in the upper portion of the stomach. Depending on the stage of the cancer, other organs or tissues close to the cancerous part of the stomach may also be removed, including the omentum (a layer of fatty tissue that covers the stomach and intestines), the spleen or portions of the esophagus or small intestine.

A subtotal gastrectomy includes a step that allows the digestive tract to continue to function. If the lower portion of the stomach has been removed, the surgeon connects the upper portion of the stomach to the small intestine. If the upper portion of the stomach has been removed, the surgeon attaches the lower portion of the stomach to the esophagus.

Total gastrectomy. If the cancer has spread throughout the stomach, a total gastrectomy (the removal the entire stomach) is performed. Additionally, this type of surgery is often recommended if the cancer is located in the upper part of the stomach. In a total gastrectomy, the surgeon also removes the omentum and may remove the spleen and parts of the esophagus, intestines, pancreas and other nearby organs. The end of the esophagus is attached to part of the small intestine to allow food to continue to move through the intestinal tract.

People can sometimes have trouble taking in enough nutrition after a gastrectomy. A jejunostomy tube (J-tube) placed into the intestine at the time of surgery can help. The end of the J-tube remains outside the body, on the skin of the abdomen. Through this tube, liquid nutrition can be put directly into the intestine until the person is able to eat normally.

A D2 lymphadenectomy, in which the surgeon ensures that an adequate number of lymph nodes are removed, is performed at the same time as a subtotal or total gastrectomy.

Chemotherapy

Systemic (whole body) chemotherapy, designed to destroy cancer cells, has long been an important approach in the treatment of gastric cancer. Most systemic chemotherapy treatments for gastric cancer combine at least two drugs. In neoadjuvant (before surgery) treatment, common drug combinations include:

- Docetaxel, oxaliplatin and fluorouracil/leucovorin (FLOT)
- Oxaliplatin plus either 5-FU or capecitabine (called FOLFOX or Capeox)

The combination treatments (FLOT, FOLFOX or Capeox) may also be given as an adjuvant (after surgery) treatment. A single drug, such as 5-FU or capecitabine, is sometimes used as adjuvant treatment for people who may not be able to tolerate combination therapy.

Other chemotherapy drugs used to treat gastric cancer include paclitaxel and irinotecan.

In February 2019, the U.S. Food and Drug Administration (FDA) approved the chemotherapy combination of trifluridine/tipiracil Lonsurf) for the treatment of metastatic (advanced) adenocarcinoma treated with at least two previous chemotherapy regimens (courses of treatment). Trifluridine works by stopping the growth of cancer cells, while tipiracil helps the trifluridine work longer by stopping it from being broken down by the body. This chemotherapy combination is taken as a pill.

Targeted Therapy

Targeted therapy focuses on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow.

There are two targeted therapies approved by the FDA for the treatment of stage IV gastric cancer:

- **Trastuzumab** (Herceptin). HER2, a growth-promoting protein found on the surface of some cancer cells, is present in approximately 20 percent of gastric cancers. Trastuzumab binds to and blocks the HER2 protein and is often added to chemotherapy for people whose cancer is HER2-positive. Trastuzumab is given intravenously (into a vein).
- **Ramucirumab** (Cyramza). VEGF (vascular endothelial growth factor) is a protein that contributes to angiogenesis (blood vessel growth), which can lead to the growth and spread of cancer. Ramucirumab blocks the action of VEGF and can be given by itself or added to paclitaxel chemotherapy. It is given intravenously.

In June 2019, the FDA approved trastuzumab-anns (Kanjinti), a biosimilar to trastuzumab, for the treatment of HER2-positive stage IV gastric cancer. Although not an exact copy of the original drug, biosimilars are expected to produce the same clinical result and have no meaningful differences in terms of safety, purity or potency.

Other targeted therapy drugs to treat gastric cancer are currently being studied in clinical trials.

Immunotherapy

Our immune system is constantly working to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

In 2017, the FDA approved the immunotherapy pembrolizumab (Keytruda) to treat certain advanced gastric cancers. The approval applies to gastric cancers that have recurred (come back) or continued to grow after at least two previous chemotherapy regimens. To be treated with pembrolizumab, the cancer cells must also test positive for the PD-L1 protein, a molecular "brake" that prevents the body's immune system from attacking cancer cells. About 60 percent of gastric cancers are PD-L1 positive.

In May 2021, the approval of pembrolizumab was further extended to the first-line treatment of locally advanced, unresectable or metastatic HER2 positive gastric cancer, in combination with trastuzumab and a specific type of chemotherapy.

Pembrolizumab, which is given intravenously, has also been approved to treat any type of cancer that has a trait known as high microsatellite instability (MSI-H), which is most frequently caused by mutations in the mismatch repair (MMR) and tumor suppression genes. A small percentage of gastric cancers are MSI-H and can be treated with pembrolizumab.

In April 2021 the FDA approved the PD-1 inhibitor nivolumab (Opdivo), in combination with chemotherapy, for the first-line treatment of advanced gastric cancer. It is of most benefit for the treatment of tumors with high levels of the PD-L1 protein.

Other immunotherapy approaches are currently being studied in clinical trials.

Antibody-drug Conjugate

An antibody-drug conjugate (ADC) is a type of anticancer treatment that combines a targeted therapy with a chemotherapy.

In January 2021, the FDA approved trastuzumab deruxtecan (Enhertu) for locally advanced or metastatic HER2-positive gastric adenocarcinoma previously treated with a trastuzumab-based regimen.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but it can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt an immune response. Because it can trigger an attack on healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, muscle pain, fever, cough, lowered levels of thyroid hormone, decreased appetite and digestive tract symptoms.

Side Effects of Antibody-drug Conjugate

The antibody drug conjugate used in the treatment of gastric cancer may cause fatigue, hair loss, anemia and digestive tract symptoms.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Constipation

- As hydration is important, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your doctor on the level of physical activity that is right for you.
- If your doctor has prescribed a "bowel regimen," make sure to follow it exactly.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

Communicating With Your Health Care Team

As you manage your gastric cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you. If you have a mobile device, ask if you can use it to take notes. Keeping notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your gastric cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of gastric cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care*® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store, or ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: Are there gene mutations or inherited conditions that increase the risk of developing gastric cancer?

A: Certain gene mutations and some inherited conditions are considered risk factors for gastric cancer, including:

- **BRCA1 and BRCA2.** Although inherited mutations on the BRCA1 and BRCA2 genes are often associated with a higher risk of breast cancer, people who have inherited these genetic mutations are also at an increased risk for gastric cancer.
- **Lynch syndrome.** Lynch syndrome is a hereditary disorder caused by a mutation in a mismatch repair gene. Most commonly Lynch syndrome is associated with an increased risk for colon cancer, but it also increases the risk of gastric and other cancers.
- **Familial adenomatous polyposis (FAP).** Often caused by mutations on the APC gene, FAP significantly increases a person's risk of colorectal cancer and may also play a smaller role in increasing the risk of developing gastric cancer.
- **E-cadherin/CDH1.** Though rare, people who inherit this genetic mutation have a significantly increased risk of developing gastric cancer in their lifetime. When this genetic mutation is present, there is often a family history of gastric cancer or lobular breast cancer, a specific type of breast cancer that begins in the milk-producing glands (lobules) of the breast.

Testing is available for gene mutations that make a person more likely to develop gastric cancer. A doctor or genetic counselor can help the individual and their family understand the test results.

Q: Is radiation used to treat gastric cancer?

A: Radiation therapy as a treatment approach for gastric cancer has become less common in recent years. It is not typically given before surgery, but can be used to destroy small traces of cancer that could not be seen and removed during surgery. Radiation can also be used if there is bleeding from the tumor. In those cases, external beam radiation is the type of radiation generally administered. External beam radiation uses a machine that directs a beam (or multiple beams) of radiation to the cancer. The use of CT (computerized tomography), MRI (magnetic resonance imaging) and PET (positron emission tomography) scans allows radiation oncologists to accurately target the cancer, helping to spare healthy tissues.

Q: What is an endoscopic resection?

A: In an endoscopic resection, the surgeon passes an endoscope (a flexible tube with a lighted video camera on the end) into the stomach through the throat. Surgical tools are then passed through the endoscope to remove the cancer and part of the stomach wall around the cancer.

Endoscopic resection is increasingly used to treat early-stage gastric cancers, where the risk of the cancer spreading to the lymph nodes is very low. If you are considering an endoscopic resection, your health care team can help you find a medical center that has experience with this surgical procedure.

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

National Comprehensive Cancer Network
215-690-0300
www.nccn.org

Debbie's Dream Foundation: Curing Stomach Cancer
855-475-1200
www.debbiesdream.org

The Gastric Cancer Foundation
www.gastriccancer.org

Medicine Assistance Tool
www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

ClinicalTrials.gov
www.clinicaltrials.gov

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

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