

Unknown Primary - Treatment Options [1]

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ON THIS PAGE: You will learn about the different ways doctors may treat this type of cancer. To see other pages, use the menu on the side of your screen.

This section outlines treatments that are the standard of care (the best proven treatments available) for CUP. When making treatment plan decisions, patients are also encouraged to consider clinical trials as an option. A clinical trial is a research study to test a new approach to treatment to evaluate whether it is safe, effective, and possibly better than the standard treatment. Clinical trials may test such approaches as a new drug, a new combination of standard treatments, or new doses of current therapies. Your doctor can help you review all treatment options. For more information, see the [Clinical Trials](#) [3] and [Latest Research](#) [4] sections.

Planning treatment

In cancer care, different types of doctors often work together to create a patient's overall treatment plan that combines different types of treatments. This is called a [multidisciplinary team](#) [5].

Answers to the following questions are very important for helping doctors plan treatment for CUP:

- Was the primary site found during clinical and imaging testing? If so, treatment should follow guidelines for an advanced (metastatic) tumor of that primary tumor type.
- Did the pathologist identify a primary tumor or a specific tumor type, such as lymphoma or germ cell tumor? If so, treatment should follow guidelines for the specific tumor type.
- If no primary site was found, does this CUP fit into any of the subgroups for which specific treatment is recommended? (Subgroups are listed below.)
- If no primary site was found and this CUP does not fit into any of the specific subgroups, will disease-directed treatment be beneficial? If so, should treatment be based on the tumor type predicted by molecular tumor profiling, or should it be with an empiric (general) chemotherapy program (see below)? The chance that chemotherapy will be effective depends on the location of the tumor, number of tumors involved, and the person's overall health.

Treatment overview

Descriptions of the most common treatment options for CUP are listed below, followed by an outline of treatment by the CUP subgroup or if a subgroup is unknown.

Chemotherapy is the most common treatment for CUP, and it may get rid of some tumors completely. Since CUP has usually spread to more than one place when diagnosed, this type of tumor can rarely be removed surgically or treated with localized radiation therapy. Your care plan may also include treatment for symptoms and side effects, which is an important part of cancer care. Take time to learn about all of your treatment options and be sure to ask questions about things that are unclear. Also, talk about the goals of each treatment with your doctor and what you can expect while receiving the treatment. Learn more about [making treatment decisions](#) [6].

For many patients, a diagnosis of CUP can be very stressful and, at times, difficult to bear. Patients and their families are encouraged to talk about the way they are feeling with doctors, nurses, social workers, or other members of the health care team. It may also be helpful to talk with other patients, including through a support group.

Chemotherapy

Chemotherapy is the use of drugs to destroy cancer cells, usually by stopping the cancer cells' ability to grow and divide. Chemotherapy is given by a medical oncologist, a doctor who specializes in treating cancer with medication.

Systemic chemotherapy is delivered through the bloodstream to reach cancer cells throughout the body. Common ways to give chemotherapy include an intravenous (IV) tube placed into a vein using a needle or in a pill or capsule that is swallowed (orally). A chemotherapy regimen (schedule) usually consists of a specific number of cycles given over a set period of time. A patient may receive one drug at a time or combinations of different drugs at the same time. The medications used to treat cancer are continually being evaluated.

The side effects of chemotherapy depend on the individual and the dose used, but they can include fatigue, risk of infection, nausea and vomiting, hair loss, loss of appetite, and diarrhea. These side effects usually go away once treatment has finished.

Learn more about [chemotherapy](#) [7] and [preparing for treatment](#) [8]. Talking with your doctor is often the best way to learn about the medications you've been prescribed, their purpose, and their potential side effects or interactions with other medications. Learn more about your prescriptions by using [searchable drug databases](#) [9].

Radiation therapy

Radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. A doctor who specializes in giving radiation therapy to treat cancer is called a radiation oncologist. A radiation therapy regimen (schedule) usually consists of a specific number of treatments given over a set period of time.

The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. When radiation treatment is given using

implants, it is called internal radiation therapy or brachytherapy.

Side effects from radiation therapy may include fatigue, mild skin reactions, upset stomach, and loose bowel movements. Most side effects go away soon after treatment is finished. Learn more about [radiation therapy](#) [10].

Surgery

Surgery is the removal of the tumor and surrounding tissue during an operation. A surgical oncologist is a doctor who specializes in treating cancer using surgery. The extent and location of the surgery depends on where the cancer is found and its size. Learn more about [cancer surgery](#) [11].

Targeted therapy

Targeted therapy is a treatment that targets the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment blocks the growth and spread of cancer cells while limiting damage to healthy cells.

A number of targeted cancer therapies are approved by the U.S. Food and Drug Administration (FDA) to treat specific cancer types, and most of the new cancer drugs currently being tested are targeted agents. Although none of them are currently approved to treat CUP, the ability to accurately predict where the tumor started in patients diagnosed with CUP may also help identify a targeted drug likely to be of benefit. For example, if a cancer is predicted to have started in the lung, it may respond to one of the targeted therapies currently approved for lung cancer.

Talk with your doctor about possible side effects for a specific medication and how they can be managed. Learn more about [targeted treatments](#) [12].

Hormone therapy

The goal of hormone therapy is to alter the activity of hormones in the body, usually trying to lower their levels or block their actions. Hormone therapy may be given to help stop the tumor from growing or to relieve symptoms caused by the tumor. This type of treatment may be an option for people in specific CUP subgroups (see below).

Treatment options for specific subgroups

The following subgroups can often be identified during the initial clinical and pathologic evaluation and have specific treatments that are often recommended.

Women with adenocarcinoma located only in the axillary lymph nodes. Treatment should follow guidelines for [stage II breast cancer](#) [13], even if no primary site in the breast can be found. Local treatment should include surgical removal of the breast (mastectomy) or surgical removal of the lymph nodes (axillary node dissection) plus radiation therapy to the breast. After surgery, chemotherapy and/or hormone therapy should also be recommended, depending on the number of lymph nodes with cancer, the estrogen/progesterone receptor (ER/PR) status, the HER2 status, and other features of the tumor.

Women with peritoneal carcinomatosis (adenocarcinoma on the surface of the abdominal cavity). Treatment should follow guidelines for stage III ovarian cancer [14], even for women with normal ovaries or whose ovaries have been removed. Whenever possible, surgery to remove as much of the cancer as possible, known as debulking surgery, should be performed. Chemotherapy with a taxane/platinum combination, which is used in the treatment of ovarian cancer, is recommended after surgery. CA-125 is often a useful tumor marker for monitoring how well treatment is working. Approximately 20% to 25% of women live for a long time after treatment.

Young men with poorly differentiated carcinoma found in the mediastinum (center of the chest between the lungs) or retroperitoneum (back of the abdominal cavity). Some men in this group may have a germ cell tumor, even if the diagnosis cannot be made by the pathologist. High levels of HCG and AFP in the blood strongly suggest a germ cell tumor [15]. Initial chemotherapy should follow guidelines for treatment of later-stage testicular cancer [16]. Removal of the remaining tumor after chemotherapy is often needed. About 30% of men in this group have the cancer successfully treated.

Squamous cell carcinoma in the cervical (neck) lymph nodes. Even if a primary site in the head and neck is not found after a careful search, these patients generally receive treatment according to guidelines for locally advanced head and neck cancer [17]. This usually includes radiation therapy and chemotherapy given at the same time. For some patients with small cervical lymph nodes with cancer, treatment with radiation therapy alone or surgery followed by radiation therapy is enough. About 40% to 60% of patients in this group live a long time after treatment.

Squamous cell carcinoma in the inguinal (groin) lymph nodes. Local treatment should include surgical removal of all inguinal lymph nodes (lymph node dissection) or radiation therapy. Combining chemotherapy at the same time as radiation therapy should also be considered.

Patients who have only a single metastasis. This includes a broad range of patients, since the single metastasis may be found in any part of the body, such as the lymph nodes, brain, lung, or liver. Depending on the location, treatment should include either surgical removal of the tumor or radiation therapy. Most patients in this group eventually develop metastases in other parts of the body, but this sometimes occurs after a long time without any disease.

Men with metastases only in the bones and/or an elevated PSA level. Treatment should follow guidelines for advanced prostate cancer [18]. Treatment with hormone therapy (androgen deprivation) frequently produces long remissions. A remission is the disappearance of the signs and symptoms of CUP.

Patients with adenocarcinoma in the liver and/or abdomen. In some patients where the tumor spread is only in the abdomen, special pathology tests (IHC stains or molecular profiling) suggest that the cancer started in the colon. Patients should receive treatment following guidelines for later-stage colon cancer [19], even if a primary site cannot be located by a colonoscopy.

Patients with poorly differentiated neuroendocrine tumors. Although the primary site is

usually not found, these types of neuroendocrine tumors [20] often respond to chemotherapy with platinum/etoposide (Etopophos), with or without taxane (docetaxel [Taxotere] or paclitaxel [Taxol]). This treatment can effectively shrink the cancer and improve cancer-related symptoms for about 60% of patients. A smaller percentage of patients in this group, about 10% to 15%, have complete remission with chemotherapy, and some live for a long time after treatment.

Patients with well-differentiated neuroendocrine tumors. Most well-differentiated neuroendocrine tumors, such as carcinoid tumors [21] or islet cell tumors [22], begin in the intestinal tract or pancreas. In patients with an unknown primary site, the metastases are usually found in the liver. It is usually easy for the pathologist to tell the difference between well-differentiated and poorly differentiated neuroendocrine tumors. This distinction is important because the chemotherapy recommended for poorly differentiated neuroendocrine tumors is usually ineffective against well differentiated tumors. Well differentiated neuroendocrine tumors usually grow slowly, and patients often live for several years even without treatment. Treatment should follow guidelines for advanced carcinoid tumors.

Treatment for those not in a specific CUP subgroup

About 75% of all people with CUP do not have the characteristics of any of the specific subgroups discussed previously. Most of the patients in this group have adenocarcinoma or poorly differentiated carcinoma. The success of treatment for this group of patients varies widely. Many of these patients have cancers that are resistant to treatment; however, others experience significant benefit.

The recommendations for treatment in this group are in the process of changing based on ongoing scientific findings. Until recently, standard treatment typically included a generalized chemotherapy approach referred to as empiric chemotherapy. This approach uses a combination of drugs traditionally known to work against a variety of cancers. Previously, the treatment of many types of advanced cancers has often been similar to each other, and so this type of approach has offered the best chance of success in many cases. Although only about 5% of patients are cured with this approach, it can shrink tumors in 35% to 40% of patients, and 20% to 25% of patients live for at least two years after diagnosis.

During the last 15 years, important improvements have been made in the treatment of many types of cancer. Many of the drugs responsible for these improvements are called targeted therapies (see above). Unlike many of the traditional chemotherapy drugs, these drugs work best for specific types of cancer with specific tumor features. For example, a drug that targets a tumor abnormality specific to lung cancer may not work at all against colon cancer, and vice versa. Therefore, it is increasingly difficult to design an empiric/generalized treatment program for patients with CUP that provides the best coverage for various cancer types.

At the same time, new diagnostic tests are now available that can predict the site of tumor origin in patients with CUP, even when the site cannot be found by scans and other clinical evaluation. These new tests, called molecular tumor profiling assays, are performed on tumor tissue taken during the biopsy. Increasing scientific evidence shows the predictions from these assays are accurate in most cases.

Although scientific evidence is not complete, it now appears that treatment based on the results

of molecular profiling offers advantages over empiric chemotherapy. For example, a patient predicted to have a site of tumor origin in the colon would receive greater benefit from treatment specifically for later-stage colon cancer, which includes targeted agents developed specifically for colon cancer, than from a generalized chemotherapy regimen traditionally used for CUP. Currently, all of the information from clinical trials consistently shows better treatment outcomes with treatment guided by molecular profiling prediction than with empiric chemotherapy.

All patients with CUP are encouraged to talk with their doctor about participating in a [clinical trial](#) [3] that is evaluating new drugs or drug combinations. In addition, talk with your doctor about the possible side effects and goals of each treatment option.

Getting care for symptoms and side effects

Cancer and its treatment often cause side effects. In addition to treatment to slow, stop, or eliminate the cancer, an important part of cancer care is relieving a person's symptoms and side effects. This approach is called palliative or supportive care, and it includes supporting the patient with his or her physical, emotional, and social needs.

Palliative care can help a person at any stage of illness. People often receive treatment for the cancer and treatment to ease side effects at the same time. Even for patients whose tumors do not respond to chemotherapy, treatments are available to reduce symptoms. In fact, patients who receive both often have less severe symptoms, better quality of life, and report they are more satisfied with treatment.

Palliative treatments vary widely and often include medication, nutritional changes, relaxation techniques, and other therapies. You may also receive palliative treatments similar to those meant to eliminate the cancer, such as chemotherapy, surgery, and radiation therapy. Talk with your doctor about the goals of each treatment in your treatment plan.

Before treatment begins, talk with your health care team about the possible side effects of your specific treatment plan and supportive care options. And during and after treatment, be sure to tell your doctor or another health care team member if you are experiencing a problem so it is addressed as quickly as possible. Learn more about [palliative care](#) [23].

Remission and the chance of recurrence

A remission is when cancer cannot be detected in the body and there are no symptoms. This may also be called "no evidence of disease" or NED. For patients who receive chemotherapy and experience remission, treatment is usually stopped after four to six months.

A remission can be temporary or permanent. This uncertainty leads to many survivors feeling worried or anxious that the cancer will come back. While many remissions are permanent, it's important to talk with your doctor about the possibility of the cancer returning. Understanding the risk of recurrence and the treatment options may help you feel more prepared if the cancer does return. Learn more about [coping with the fear of recurrence](#) [24].

If the cancer does return after the original treatment, it is called recurrent cancer. It may come back in the same place or in other areas of the body. When this occurs, a cycle of testing will

begin again to learn as much as possible about the recurrence. After testing is done, you and your doctor will talk about your treatment options.

Chemotherapy will usually be recommended, either with the same drugs you received before or with a new combination. If your first treatment was based on the tumor type predicted by molecular tumor profiling, second-line treatment will likely continue to follow the standard treatment for that tumor type. Your doctor may also suggest clinical trials that are studying new ways to treat this type of recurrent cancer.

People with recurrent cancer often experience emotions such as disbelief or fear. Patients are encouraged to talk with their health care team about these feelings and ask about support services to help them cope. Learn more about [dealing with cancer recurrence](#) [25].

If treatment fails

Recovery from cancer is not always possible. If treatment is not successful, the disease may be called advanced or terminal cancer.

This diagnosis is stressful, and this is difficult to discuss for many people. However, it is important to have open and honest conversations with your doctor and health care team to express your feelings, preferences, and concerns. The health care team is there to help, and many team members have special skills, experience, and knowledge to support patients and their families. Making sure a person is physically comfortable and free from pain is extremely important.

Patients who have advanced cancer and who are expected to live less than six months may want to consider a type of palliative care called hospice care. Hospice care is designed to provide the best possible quality of life for people who are near the end of life. You and your family are encouraged to think about where you would be most comfortable: at home, in the hospital, or in a hospice environment. Nursing care and special equipment can make staying at home a workable alternative for many families. Learn more about [advanced cancer care planning](#) [26].

After the death of a loved one, many people need support to help them cope with the loss. Learn more about [grief and loss](#) [27].

The next section helps explain clinical trials, which are research studies. Use the menu on the side of your screen to select About Clinical Trials, or you can select another section, to continue reading this guide.

Links:

- [1] <http://www.cancer.net/cancer-types/unknown-primary/treatment-options>
- [2] <http://www.cancer.net/about-us>
- [3] <http://www.cancer.net/node/19693>
- [4] <http://www.cancer.net/node/19696>
- [5] <http://www.cancer.net/node/25356>
- [6] <http://www.cancer.net/node/24582>
- [7] <http://www.cancer.net/node/24723>
- [8] <http://www.cancer.net/node/24473>
- [9] <http://www.cancer.net/node/25369>
- [10] <http://www.cancer.net/node/24728>

- [11] <http://www.cancer.net/node/24720>
- [12] <http://www.cancer.net/node/24729>
- [13] <http://www.cancer.net/node/18626>
- [14] <http://www.cancer.net/node/19488>
- [15] <http://www.cancer.net/node/29861>
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- [17] <http://www.cancer.net/node/18915>
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- [19] <http://www.cancer.net/node/18708>
- [20] <http://www.cancer.net/node/19443>
- [21] <http://www.cancer.net/node/18645>
- [22] <http://www.cancer.net/node/18941>
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