Unknown Primary - Treatment

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Treatment Options

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 treatment to evaluate whether it is safe, effective, and possibly better than standard treatment. Your doctor can help you review all treatment options. For more information, see the Clinical Trials [2] and Current Research [3] sections.

Treatment overview

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 [4].

Descriptions of the most common treatment options for CUP are listed below, followed by an outline of treatment by the CUP subgroup. 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. Learn more about making treatment decisions [5].

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 kill cancer cells, usually by stopping the cancer cells' ability to grow and divide. Most chemotherapy drugs are injected intravenously (into a vein), but a few are taken by mouth (orally). These drugs circulate in the bloodstream to reach cancer cells throughout the body. Chemotherapy is given by a medical oncologist, a doctor who specializes in treating cancer with medication. 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 side effects of chemotherapy depend on the individual and the dose used, but they can include fatigue, risk of infection, nausea and vomiting, loss of appetite, and diarrhea. These side effects usually go away once treatment is finished.

The medications used to treat cancer are continually being evaluated. Learn more about chemotherapy [6] and preparing for treatment [7]. 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 [8].

Radiation therapy

Radiation therapy is the use of high-energy x-rays or other particles to kill 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 [9].

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. During surgery, the surgical oncologist removes the tumor and an area of tissue around the tumor (called a margin). The extent and location of the surgery depends on where the cancer is found and its size. Learn more about cancer surgery [10].

Treatments by CUP subgroup

The following subgroups can often be identified during the initial clinical and pathologic evaluation (see Diagnosis [11]) and have recommended treatments:

Women with adenocarcinoma located only in the axillary lymph nodes. Treatment should follow guidelines for stage II breast cancer [12], even if no primary site in the breast can be found. Local treatment should include mastectomy (surgical removal of the breast) or axillary node dissection (surgical removal of the lymph nodes) plus radiation therapy to the breast. Adjuvant treatment (treatment after surgery) with 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 [13], even for women with normal ovaries or whose ovaries have been removed. When possible, debulking surgery (surgery to remove as much of the cancer as possible) should be performed. Chemotherapy with a taxane/platinum combination is recommended after surgery, which is similar to ovarian cancer treatment. CA-125 is often a useful tumor marker for monitoring how well treatment is working. Approximately 20% to 25% of women live 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 germ cell tumors, even if the diagnosis cannot be made. High levels of HCG and AFP in the blood strongly suggest a germ cell tumor [14]. Initial chemotherapy should follow guidelines for treatment of advanced testicular cancer [15]. 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 in a careful search, these patients should receive treatment according to guidelines for locally advanced head and neck cancer [16]. 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 a lymph node dissection (removal of all inguinal lymph nodes) 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 (for example, 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 often after a long time without any disease.

Men with metastases only in the bones and/or an elevated PSA level. These patients should be treated with hormone therapy, similar to the treatment recommendations for advanced prostate cancer [17].

Patients with adenocarcinoma in the liver and/or abdomen. In some patients where the tumor spread is only in the abdomen, special pathology tests suggest that the cancer started in the colon. Patients should receive treatment following guidelines for advanced colon cancer [18], even if a primary site cannot be located by colonoscopy.

Patients with poorly differentiated neuroendocrine tumors. Although the primary site is usually not found, these types of neuroendocrine tumors [19] often respond to chemotherapy with platinum/etoposide (Etopophos), with or without taxane (paclitaxel [Taxol] or docetaxel [Taxotere]). This treatment can effectively shrink the cancer and improve cancer-related symptoms for about 60% of patients. A smaller percentage (10% to 15%) of patients in this group has complete shrinkage of cancer with chemotherapy.

Patients with well differentiated neuroendocrine tumors. Most well differentiated neuroendocrine tumors (such as carcinoid [20] or islet cell tumors [21]) arise in the intestinal tract or pancreas. In patients with an unknown primary site, the tumor usually spreads to 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 these tumors. Well differentiated neuroendocrine tumors typically grow slowly, and patients often live for several years even without treatment. Treatment should follow guidelines for advanced carcinoid tumors.

Patients with poorly differentiated carcinoma. Patients in this group have tumors of many types, and chemotherapy sometimes works well. Patients with certain clinical factors (such as tumors located only in lymph nodes, two or fewer areas of metastasis, and younger age) have better outcomes with chemotherapy. Clinical trials should be offered to all patients in this group.

Treatment for those not in a CUP subgroup

For a patient whose CUP does not fall into any of the subgroups above, treatment is often less effective. However, many patients can benefit in some way from chemotherapy. Several combinations of chemotherapy have been researched and evaluated in patients with CUP. Usually, these chemotherapy treatment plans contain drugs known to be effective against a variety of cancer types. In particular, combination chemotherapy

containing newer drugs has been shown to be more effective and have fewer side effects.

Although chemotherapy cures only about 5% of these patients, it can shrink tumors for about 35% to 40% of patients, and 20% to 25% of patients live two years or more after diagnosis. After about four to six weeks of treatment, it is clear which patients are benefiting from treatment; those patients will continue treatment for four to six months.

All patients with CUP should talk with their doctor about participating in a clinical trial [2] that is evaluating new drugs or drug combinations. Many new drugs are being studied, and it is likely that some of these will improve the treatment of patients with CUP.

Palliative/supportive care

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.

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.

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 [22].

Recurrent CUP

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 [23].

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. 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 [24].

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.

Palliative care given toward the end of a person's life is called hospice care [25]. 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 cope with the loss. Learn more about grief and bereavement [27].

Find out more about common terms used during cancer treatment [28].

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/19693
[3] http://www.cancer.net/node/19696
[4] http://www.cancer.net/node/25356
[5] http://www.cancer.net/node/24582
[6] http://www.cancer.net/node/24723
[7] http://www.cancer.net/node/24473
[8] http://www.cancer.net/node/25369
[9] http://www.cancer.net/node/24728
[10] http://www.cancer.net/node/24462
[11] http://www.cancer.net/node/19691

[12] http://www.cancer.net/node/18626
[13] http://www.cancer.net/node/19488
[14] http://www.cancer.net/node/25752
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