

TREATMENT INFORMATION SERIES

Systemic Therapy

CHORDOMA FOUNDATION

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The Chordoma Foundation is committed to helping patients and caregivers make the most informed treatment decisions. We created the Treatment Information Series to provide you with in-depth information about each aspect of treatment that may be involved in your chordoma journey. The complete series, as well as other materials for patients and caregivers, is available at **chordoma.org/educational-materials**.

Understanding systemic therapy

Systemic therapy is the use of treatments that spread throughout the body to kill cancer cells wherever they are located. These treatments are prescribed by doctors called medical oncologists or neuro-oncologists. Systemic therapy includes different types of drugs and treatments, such as chemotherapy, targeted therapy, and immunotherapy. Since surgery and radiation are the recommended treatments for newly diagnosed chordoma, systemic therapy is usually only used to treat locally advanced or metastatic chordoma.

Chemotherapy

In general, chemotherapy drugs work by targeting DNA and other structures in cancer cells. Chemotherapy drugs cannot tell the difference between cancer cells and healthy cells, however, which is why side effects occur. These can include low blood counts, hair loss, nausea, fatigue, or damage to organs. If you are treated with chemotherapy, your oncologist will monitor you for these side effects. Chemotherapy treatments are most commonly given intravenously (IV) but can be given orally as well.

Conventional and chondroid chordomas are typically resistant to chemotherapy drugs. For this reason, chemotherapy is not routinely used to treat these types of chordoma. However, there is some published evidence that sarcoma chemotherapy regimens may be effective in treating the poorly differentiated and dedifferentiated types of chordoma, which occur more often in pediatric and young adult patients and usually grow faster than the other types. These regimens include the drugs doxorubicin, ifosfamide, etoposide, vincristine, cyclophosphamide, and cisplatin.

Read more about chordoma in children and young adults at **chordoma.org/pediatric**



Targeted therapy

Targeted therapies are designed to target the changes and mutations found in cancer cells. Every patient's tumor cells have unique changes in the DNA and RNA within the cells, which allow the cells to grow uncontrollably and spread. Targeted therapies work by acting against those changes in a way that will cause the cells to die. They are typically given orally and sometimes intravenously (IV). These treatments can cause side effects including vomiting, diarrhea, liver problems, high blood pressure, mouth sores, and issues with hair, skin, and nails. There are medications that can help prevent or treat these side effects in many cases.

Many chordoma patients with metastatic or advanced disease are treated with targeted therapies to keep their tumors from progressing further. The chance of significant tumor shrinkage is low, but some patients' tumors remain stable while taking the drug. One drawback of targeted therapy is that cancer cells can become resistant to them, so in some cases they are combined with chemotherapy, immunotherapy, or radiation.

Immunotherapy

The immune system includes cells, tissues, and organs that help the body fight infection and disease. One reason tumors continuously grow and divide without being killed by the immune system is because tumor cells are very effective at being able to "hide" from the immune system. Immunotherapies are treatments that help your immune system find and kill tumor cells. Different types of immunotherapy use different components of the immune system to fight cancer.



Checkpoint inhibitors help the immune system by "releasing the brakes" that keep immune cells from being able to find tumor cells. They work by interfering with proteins produced by tumor cells that allow them to avoid attack by the immune system.



Therapeutic vaccines use substances the immune system recognizes as foreign to the body, similar to a flu shot. The immune response to these substances helps stimulate response to tumor cells.



Adoptive cell transfer uses the patient's own immune cells to fight the tumor cells. Immune cells are taken from the patient's tumor and genetically modified to learn to attack the cancer cells. The genetically modified cells are allowed to grow in a lab over a few weeks. Once there are a large number of the tumor-fighting immune cells, they are injected back into the patient's body intravenously.

Immunotherapy will play an increasingly important role in cancer treatment in the future, and it is currently being studied in clinical trials for the treatment of chordoma.



For a list of targeted therapies and immunotherapies relevant to chordoma treatment visit **chordoma.org/systemic-therapy**



Length of treatment

Typically, doctors will continue to treat patients with a therapy until the tumor grows significantly, which suggests the treatment is not working or has stopped working, or until there are side effects that make the treatment intolerable. How long a patient continues with a particular therapy varies based on the individual patient's situation. If your doctors discontinue a therapy for one of these reasons, they will typically work with you to find another to try.

Possible side effects

All systemic therapies have the risk of potential side effects, ranging from mild to severe.

- **Chemotherapy:** low blood counts, hair loss, nausea, fatigue, and organ damage
- **Targeted therapy:** vomiting, diarrhea, liver problems, high blood pressure, mouth sores, and issues with hair, skin, and nails
- **Immunotherapy:** infection-like symptoms, allergic reactions, and auto-immune disorders (where the body attacks normal tissues like the liver, kidneys, lung, skin, pancreas, and other organs). Though serious side effects are less common, they can be extremely severe and life threatening when they do happen.

Any new side effects experienced while taking a systemic therapy, whether in a clinical trial or off-label, should be reported to your doctor immediately.

Considering systemic therapy for chordoma

Chordoma patients whose tumors have come back (recurrent disease) or spread to other parts of the body (metastatic disease) may consider systemic therapies when treatment with surgery and/or radiation are not possible or not recommended. Systemic therapies may also be considered if the tumor is growing rapidly, or if it has been determined that the tumor is either the poorly differentiated or dedifferentiated type of chordoma.

Currently, no systemic therapies have been approved by government regulatory agencies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) for the treatment of chordoma. However, in some countries, doctors can still prescribe treatments to chordoma patients that have been approved for other cancers. This is called "off-label" use of the treatment.



For more information about systemic therapy, contact a Chordoma Foundation Patient Navigator at **chordoma.org/request-help**

Cost of systemic therapy treatments

When doctors prescribe systemic therapies off-label, they are typically not paid for by insurance or by health systems. However, this varies widely, so it is important to check with your insurance provider or health system. On occasion, drug companies have programs that make their treatments available to patients at minimal or no cost. These programs are called "compassionate use" or "expanded access". It may also be possible for chordoma patients to receive certain therapies by participating in clinical trials.

Medical Advisory Board recommendations

Though each patient's situation is unique, in general, the Chordoma Foundation Medical Advisory Board (MAB) recommends that individuals with recurrent or advanced disease pursue treatment options in the following order of priority:

1. **Chordoma-specific clinical trials**
   Start by considering trials designed specifically for chordoma patients. These trials are likely to have strong scientific justification and to be conducted by teams with significant experience caring for chordoma patients.
2. **Other relevant clinical trials recommended by an experienced physician**
   If you are not eligible for any chordoma-specific trials, ask your oncologist about other clinical trials that may be open to you.
3. **Off-label therapy with evidence of clinical benefit for chordoma patients**
   While there are currently no drugs approved for the treatment of chordoma, some drugs that are approved for the treatment of other cancers have shown modest activity in chordoma patients. In some countries, doctors can choose to prescribe these drugs to chordoma patients if they believe they will be of benefit. This is called "off-label" use. If you are not eligible for any clinical trials, consult with your oncologist about off-label use of approved drugs that have been used to treat chordoma patients.


For a list of trials enrolling chordoma patients, visit our Clinical Trials Catalogue at **chordoma.org/clinical-trials**


Learn more about systemic therapy for chordoma at **chordoma.org/systemic-therapy**



Personalized medicine

Personalized medicine — also called precision medicine or personalized oncology — uses information about a person's genetics and other characteristics to prevent, diagnose, and treat disease. Personalized medicine in cancer treatment involves testing a patient's tumor cells to learn more about the tumor's genetic alterations. Doctors then use this information to decide which treatment is best for that particular patient. Personalized medicine is routinely used in certain cancers such as breast and lung cancer and has shown promise in many others.

Genomic profiling tests

Genomic profiling provides information about the genetic makeup of cancer cells. To get this information, a small piece of tumor tissue from a recent surgery or biopsy is sent to a lab where the DNA – and sometimes RNA, depending on the test – of the cancer cells is analyzed in order to identify changes and alterations.

A report is generated with the results of the test. In some cases, an actionable target is found — in other words, the test finds a mutation in the patient's tumor cells that can be targeted by a certain drug or immunotherapy. In other cases, no actionable mutations are found or the mutations found do not have accessible treatments — for example, the treatment is only available through a clinical trial but the patient is not eligible for the trial.

Some clinical trials offer genomic profiling as part of the trial, and profiling tests are also available through some major medical centers. Several private companies also offer tumor profiling services. For U.S. patients, some insurance plans pay for the tests, and Medicaid and Medicare now cover them fully. The private companies may offer financial assistance to patients who are uninsured, or cannot afford the cost of testing. In some countries, the government health system may pay for profiling tests.

Testing chordoma tumors

Many chordoma patients considering systemic therapy options are offered or can request genomic profiling tests. A recent tumor sample is best for testing, but the tests can usually also be done on tissue stored after a previous surgery if a recent sample is not available.

For many cancers, including chordoma, there is no certainty that the results of tumor profiling tests will be able to help guide treatment decisions. Discussing the pros and cons of testing with your medical oncologist can help you make the best decision for your individual situation.

Some points to consider with your doctors might include:

- What tests are available to me and which one will provide the most information? How will treatment recommendations be made if the tests do not provide actionable results?
- (If you are thinking about enrolling in a clinical trial) How much tumor tissue is available for testing? Will any tissue be required to determine my eligibility for a trial? Is there enough tissue for both genomic testing and clinical trials? Can the trial doctors use the results of the testing to determine my eligibility?
- Will the cost be fully covered by my insurance plan or health system? Is a payment plan available to help with out-of-pocket costs? Is it possible to learn about potential targets through less expensive tests like immunohistochemistry (IHC)?



For a list of questions that can help you think about what you might want to ask your doctors about systemic therapy and genomic profiling, visit **chordoma.org/treatment-questions**

How we can help

The Chordoma Foundation Patient Navigation Service is here to help. Our dedicated Patient Navigators are available to:

- Answer questions about chordoma
- Provide information on treatment guidelines, experienced physicians, and treatment centers
- Identify and provide information on clinical trials open to chordoma patients, and other options for systemic therapy
- Give referrals to programs and organizations that offer travel and lodging assistance, co-pay relief, and other benefits
- Support requests and appeals to insurance companies
- Connect you with other patients and caregivers in the chordoma community



Learn more about the Patient Navigation Service at **chordoma.org/patient-navigation**

Learn more

Visit the Chordoma Foundation at **chordoma.org** for more information on chordoma, including research updates, the latest news on treatments, and ways to get involved.

Get help from a Chordoma Foundation Patient Navigator at **chordoma.org/request-help** or by calling (888) 502-6109.

Connect with other patients and caregivers through the Chordoma Connections online community at **community.chordoma.org**.

Important note about this publication

The content herein was developed by the Chordoma Foundation in consultation with members of our Medical Advisory Board. It is not meant to take the place of medical advice. You should always talk with your doctors about treatment options and decisions.

We would like to the thank the members of our Medical Advisory Board for providing their expertise in contributing to the content and review of our educational materials:

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