

Treating Malignant Mesothelioma

If you've been diagnosed with malignant mesothelioma, your cancer care team will discuss your treatment options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is mesothelioma treated?

The main factors in selecting treatment for mesotheliomas are the location and extent of the tumor, whether it has spread to lymph nodes or other organs, and your health and personal preferences. Based on these factors, your treatment options may include:

- Surgery for Malignant Mesothelioma
- Palliative Procedures for Malignant Mesothelioma
- Radiation Therapy for Malignant Mesothelioma
- Chemotherapy for Malignant Mesothelioma

of mesothelioma patients at major medical centers.

• Treatment of Mesothelioma Based on the Extent of the Cancer

Who treats mesothelioma?

You might have different types of doctors on your treatment team, depending on the stage of your cancer and your treatment options. These doctors may include:

- A **thoracic surgeon:** a doctor who treats diseases of the lungs and chest with surgery
- A surgical oncologist: a doctor who treats cancer with surgery
- A radiation oncologist: a doctor who treats cancer with radiation therapy.
- A **medical oncologist:** a doctor who treats cancer with medicines such as chemotherapy
- A **pulmonologist:** a doctor who specializes in medical treatment of diseases of the lungs

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

Health Professionals Associated with Cancer Care

Making treatment decisions

Before deciding on a treatment plan, it's very important to have an idea of its likely benefits and possible risks. You will probably have many questions about the treatment options suggested. If there's anything you don't understand, ask to have it explained.

Mesotheliomas are rare, so if time allows it's often a good idea to get a second opinion from a doctor who has a lot of experience in treating people with these cancers. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- Questions to Ask About Malignant Mesothelioma
- <u>Seeking a Second Opinion</u>

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-ofthe art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

<u>Clinical Trials</u>

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

<u>Complementary and Integrative Medicine</u>

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an

important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors and you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Surgery for Malignant Mesothelioma

Types of surgery for pleural mesothelioma

- Surgery for peritoneal mesothelioma
- Surgery for pericardial mesothelioma
- Surgery for mesothelioma of the tunica vaginalis
- More information about Surgery

Surgery for mesothelioma may be done:

- To try to cure the cancer (potentially curative surgery)
- To relieve pain and other symptoms caused by the tumor (palliative surgery)

Potentially curative surgery may be an option if you're in otherwise good health and the cancer can be removed completely. But even when the surgeon removes all of the cancer that can be seen, some cancer cells are often left behind. These cells can grow and divide, causing the cancer to come back after surgery. Because of this, not all doctors agree on the exact role of surgery. In most cases it won't cure you, but it could help you live longer. Still, potentially curative surgery is being done in some major cancer centers, and a small number of people who have had the surgery have had long periods of time with no sign of cancer.

Palliative surgery may be an option if the tumor has already spread beyond where it started and would be hard to remove completely. It may also be used if you're too ill for a more extensive operation. The goal of this surgery is to ease or prevent symptoms, not to cure the cancer.

Types of surgery for pleural mesothelioma

Either potentially curative or palliative surgery might be used for pleural mesothelioma. But in most cases, these tumors have spread too far to be removed completely. Sometimes, the surgeon might not be able to tell the full extent of the cancer – and not know which type of surgery might be best – until the operation has started.

Extrapleural pneumonectomy (EPP): This is a major operation, but it may offer the best chance to remove all of the cancer for many patients. It might be used when the surgeon thinks a cure is possible – mostly in patients with resectable epithelioid mesothelioma that has not spread to the lymph nodes.

In EEP, the surgeon removes the lung on the side of the cancer along with the pleura lining the chest wall on that side, the diaphragm (thin breathing muscle) on that side, maybe the pericardium (the sac around the heart), and nearby lymph nodes. The diaphragm and the pericardium are then rebuilt with man-made materials.

This is a complex operation that's only done by experienced surgeons in large medical

Surgery for peritoneal mesothelioma

Surgery for peritoneal mesothelioma can be used to help ease symptoms or to remove the tumor from the wall of the abdomen (belly) and digestive organs. As is the case with pleural mesothelioma, these tumors often have spread too far to be removed completely.

Debulking: The goal of this surgery is to remove as much of the mesothelioma as possible. Sometimes this means removing pieces of the intestine as well.

After as much of the visible cancer is removed as possible (but before the operation is finished), chemotherapy may be put into the abdomen. This is called **intraoperative or intraperitoneal chemotherapy**. If the chemotherapy drugs are heated, it's called **heated intraoperative chemotherapy or HIPEC**. In either treatment, the drugs are left in for a short time, then they're removed and the incision is closed.

Omentectomy: The omentum is an apron-like layer of fatty tissue that drapes over the organs inside the abdomen. Cancers in the peritoneum often spread to this tissue, so it may be removed as part of surgery for peritoneal mesothelioma.

Surgery for pericardial mesothelioma

Surgery can remove a mesothelioma from the pericardium (the sac around the heart). The entire pericardium may be removed (called a pericardectomy) can be removed to ease pressure on the heart. Surgery may be done to make a hole in the pericardium, which is called a pericardial window. This can be used to put chemo into the area around the heart.

Surgery for mesothelioma of the tunica vaginalis

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Palliative Procedures for Malignant Mesothelioma

- Removing fluid
- Pleurodesis
- Shunt placement
- Catheter placement
- More information about palliative care

Shunt placement

A shunt is a device that allows fluid to move from one part of the body to another. For example, a pleuro-peritoneal shunt lets excess fluid in the chest drain into the abdomen (belly). There, it's more likely to be absorbed by the body. A shunt may be used if pleurodesis or other techniques don't work.

The shunt is a long, thin, flexible tube with a small pump in the middle. In the operating room, the doctor puts one end of the shunt into the chest space and the other end into the abdomen. (The pump part stays just under the skin over the ribs.) Once the shunt is in place, the patient pushes down on the pump several times to move the fluid from the chest to the abdomen. This is usually done a few times each day.

Catheter placement

This is another approach sometimes used to control fluid build-up. One end of the catheter (a thin, flexible tube) is put in the chest (or abdomen for peritoneal mesothelioma) through a small cut in the skin, and the other end is left outside the body. This is done in a doctor's office or hospital. Once in place, the catheter can be attached to a special bottle or other device to drain fluid out on a regular basis.

More information about palliative care

To learn more about how palliative care can be used to help control or reduce symptoms caused by cancer, see <u>Palliative Care³</u>.

To learn about some of the side effects of cancer or treatment and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/malignant-mesothelioma/detection-diagnosis-</u> staging/how-diagnosed.html
- 2. <u>www.cancer.org/cancer/types/malignant-mesothelioma/detection-diagnosis-</u> <u>staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/managing-cancer/palliative-care.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Bibby AC, Tsim S, Kanellakis N, et al. Malignant pleural mesothelioma: an update on investigation, diagnosis and treatment. *European Respiratory Review*. 2016;25:472-486.

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Radiation Therapy for Malignant Mesothelioma

- Types of radiation therapy
- Possible side effects
- More information about radiation therapy

Radiation therapy uses high-energy x-rays or particles to kill cancer cells. Mesotheliomas tend to be hard to treat with radiation therapy. They don't usually grow as single, distinct tumors, so it can be hard to aim radiation at them while avoiding nearby normal tissues. Still, newer techniques give better control of the radiation beams and may make this form of treatment more useful for some people.

Radiation therapy can be used in different ways to treat mesothelioma:

- It can be used after surgery to try to kill any small areas of cancer that couldn't be seen and removed during surgery. This is called **adjuvant** radiation therapy.
- It can be used as a palliative procedure to ease symptoms of mesothelioma such as shortness of breath, pain, bleeding, or trouble swallowing.

Types of radiation therapy

External beam radiation therapy (EBRT)

This is the main type of radiation therapy used for mesothelioma. It uses x-rays from a machine outside the body to kill cancer cells.

With newer techniques, for example, intensity-modulated radiation therapy (IMRT), doctors can treat mesotheliomas more accurately while reducing the radiation damage to nearby healthy tissues. This might offer a better chance of radiation working, while limiting side effects.

Brachytherapy

For this type of radiation therapy, a radiation source is put inside the body, in or near the cancer. Brachytherapy is seldom used for mesothelioma unless it's part of a <u>clinical</u> <u>trial.</u>¹

Possible side effects

Side effects of external radiation therapy include fatigue, sunburn-like skin problems, and hair loss where the radiation enters the body. These usually go away once treatment is finished. Chest radiation therapy can damage the lungs over time and lead to trouble breathing and shortness of breath. Abdominal radiation therapy may cause nausea, vomiting, diarrhea, and loss of appetite.

If radiation therapy is used together with chemotherapy, the side effects tend to be worse.

If you're having any side effects from radiation, talk with your treatment team. There are often ways to help control these symptoms.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u>².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> trials.html
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

References

American Society of Clinical Oncology. Mesothelioma: Treatment Options. 07/2017. Accessed at www.cancer.net/cancer-types/mesothelioma/treatment-options on November 2, 2018.

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Chemotherapy for Malignant Mesothelioma

- How chemotherapy is given
- Systemic chemo
- Intrapleural or intraperitoneal chemo
- Chemotherapy drugs used for mesothelioma
- Possible side effects
- More information about chemotherapy

Chemotherapy (chemo) is treatment with anti-cancer drugs. It's used in many different ways to treat mesothelioma. More studies are needed to find the best drugs and the best way to use chemo. Today, the best results are seen when it's used along with

surgery.

If mesothelioma can be treated with surgery, chemo may be given first (before surgery) to try to shrink the cancer and lower the risk that it will spread. This is called **neoadjuvant therapy**.

Chemo can also be given after surgery to try to kill any cancer cells that were left behind. This type of treatment, called **adjuvant therapy**, may help delay or help keep the cancer from growing back.

For cancers that can't be removed with surgery, chemo may be the main treatment (alone or along with radiation therapy). Chemo may shrink the cancer or slow its growth, but it's very unlikely that it will make it go away completely.

How chemotherapy is given

Doctors usually give chemo in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Chemo cycles generally last about 3 to 4 weeks. Chemo is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting it.

There are 2 main ways chemo can be given to treat mesothelioma.

Systemic chemo

In systemic therapy, chemo is injected into the blood through a vein. The drug goes into the bloodstream and travels throughout the body to reach and destroy the cancer cells wherever they may be.

Intrapleural or intraperitoneal chemo

Chemo drugs can also be put right into the body space where the cancer is – either intrapleurally (into the chest) or intraperitoneally (into the abdomen). This is done with a small catheter (tube) placed through a small cut in the chest or abdominal wall. Chemo drugs given this way are still absorbed into the bloodstream, but the highest concentrations of the drugs go right to where the cancer cells are.

For intrapleural or intraperitoneal chemo, the drugs are sometimes heated before they are put into the body space. This is called **hyperthermic chemotherapy**. Heating the chemo drugs may help them work better. Sometimes this treatment is given as a single

dose in the operating room, right after surgery is done to remove the cancer. This is called **heated intraoperative chemotherapy**. It's more often used to treat peritoneal cancers, in which case it may be called **heated intraperitoneal chemotherapy** or HIPEC.

Chemotherapy drugs used for mesothelioma

Many chemo drugs can be used to treat mesothelioma, including:

- Pemetrexed (Alimta[®])
- Cisplatin
- Carboplatin
- Gemcitabine (Gemzar[®])
- Vinorelbine

These are often given as combinations of 2 drugs. But single drugs can be used in people who may not be able to tolerate more than one drug.

When 2 drugs are used, most doctors give pemetrexed and cisplatin. Pemetrexed lowers levels of folic acid and vitamin B12 in the body, so patients get these as well to help avoid certain side effects. Other possible combinations include pemetrexed with carboplatin, or cisplatin with gemcitabine.

The drugs used for HIPEC include:

- Cisplatin plus doxorubicin (most common)
- Paclitaxel
- Pemetrexed

Possible side effects

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cell are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are likely to be affected by chemo, which can lead to side effects.

given, and how long they're used. Common side effects include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about medicines to help reduce side effects, and let them know if you have side effects, so they can be managed.

Intrapleural or intraperitoneal chemo tends to cause fewer problems than systemic chemo.

Some drugs can have other side effects. For example, cisplatin and carboplatin can damage nerves (called *peripheral neuropathy*). This can sometimes lead to hearing loss or symptoms in the hands and feet such as pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. This usually goes away over time once treatment is stopped, but it can last a long time in some people.

Be sure to report any side effects or changes you notice to your medical team so that you can get them treated right away. In some cases, the doses of the drugs may need to be reduced or treatment may need to be delayed or stopped to keep the effects from getting worse.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see <u>Chemotherapy</u>¹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

References

American Society of Clinical Oncology. Mesothelioma: Treatment Options. 07/2017. Accessed at www.cancer.net/cancer-types/mesothelioma/treatment-options on November 2, 2018.

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Immunotherapy for Malignant Mesothelioma

- Immune checkpoint inhibitors
- Side effects of checkpoint inhibitors
- More information about immunotherapy

Immunotherapy is the use of drugs to stimulate a person's own immune system so it can better recognize and destroy cancer cells.

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses "checkpoints," which are proteins on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to keep from being attacked by the immune system.

Newer drugs that target these checkpoint proteins, called *checkpoint inhibitors*, can help restore the immune response against the cancer cells.

PD-1 inhibitors

Pembrolizumab (Keytruda) and **nivolumab (Opdivo)** are drugs that target PD-1, a protein on immune system cells called *T cells*. PD-1 helps keep the T cells from attacking other cells in the body. By blocking PD-1, these drugs boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

Either of these drugs can be used in people whose mesothelioma is still growing after initial treatment. Nivolumab can also be used along with another checkpoint inhibitor, ipilimumab (see below), as the first treatment in people with mesothelioma that cannot be removed with surgery.

These drugs are given as an intravenous (IV) infusion every 2 to 6 weeks.

CTLA-4 inhibitor

Ipilimumab (Yervoy) is another drug that boosts the immune response, but it has a different target. It blocks CTLA-4, another protein on T cells that normally helps keep them in check.

This drug can be used along with nivolumab (see above) to treat advanced mesothelioma, but it's not used alone.

It's given as an intravenous (IV) infusion, usually once every 6 weeks.

Side effects of checkpoint inhibitors

Side effects of these drugs can include fatigue, cough, nausea, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often:

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting one of these drugs.

Autoimmune reactions: These drugs work by removing one of the safeguards from the body's immune system. Sometimes the immune system then starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs. These types of side effects seem to happen more often with ipilimumab than with the PD-1 inhibitors.

It's very important to report any new side effects during or after treatment with any of these drugs to your health care team right away. If serious side effects do occur, you may need to stop treatment and take high doses of corticosteroids to suppress your immune system.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>¹.

To learn about some of the side effects listed here and how to manage them,

see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Rossini M, Rizzo P, Bononi I, et al. New perspectives on diagnosis and therapy of malignant pleural mesothelioma. *Front Oncol.* 2018;8:91.

Targeted Therapy for Malignant Mesothelioma

As researchers learn more about the gene and protein changes in mesothelioma, they've tried to develop new drugs to target these changes. Many kinds of cancer are treated with targeted therapy today. Research is being done to see if they might work

may be needed to fix it.

Another rare, but serious side effect of these drugs is an allergic reaction during the infusion, which could cause breathing problems and low blood pressure. You'll be watched closely while getting targeted therapy.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>¹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

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Bibby AC, Tsim S, Kanellakis N, et al. Malignant pleural mesothelioma: an update on investigation, diagnosis and treatment. European Respiratory Review. 2016;25:472-486.

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Treatment of Mesothelioma Based on the Extent of the Cancer

- Resectable mesotheliomas
- Unresectable mesotheliomas
- Recurrent mesotheliomas

The <u>stage</u>¹ (extent) of mesothelioma is an important factor in determining treatment options. But other factors, such as whether the doctor feels the cancer is resectable (all visible cancer can be removed by surgery), as well as a person's general health and preferences, also play a role.

Mesothelioma tends to be hard to treat, whether the cancer is resectable or not. It's best to be treated by a team of doctors who have a lot of experience with mesothelioma. It's also very important that you understand the goal of treatment before it starts – whether it's to try to cure the cancer or to help relieve symptoms – as well as the possible benefits and risks. This can help you make an informed decision when looking at your treatment options.

Resectable mesotheliomas

Most stage I and some stage II and III pleural mesotheliomas are potentially resectable, but there are exceptions. Whether a tumor is resectable is also based on the <u>subtype</u>² (most doctors don't believe that sarcomatoid tumors are helped by resection), where it is in the body, how far it has grown into nearby tissues, and if the person is healthy enough to have <u>surgery</u>.

Many people with resectable pleural mesothelioma have it removed by either pleurectomy/decortication (P/D) or extrapleural pneumonectomy (EPP). Surgery is more likely to have long-term benefits in early-stage cancers, where there's a better chance that most or all of the cancer can be removed. EPP might offer the best chance to remove the cancer, but it's a complex and extensive operation that's more likely to cause complications, and not all patients can tolerate it.

Patients with early-stage peritoneal mesotheliomas might also benefit from surgery to

treatments may help people live longer, it's very unlikely that they will cure these cancers. Before starting treatment, the goals of the treatment should be clear to you and your family.

In people with early-stage mesotheliomas that are likely to grow slowly and aren't causing any symptoms, watching the cancer closely at first may be a reasonable option. Treatment can then be started if there are signs that the cancer is growing quickly or if it starts to cause symptoms.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/malignant-mesothelioma/detection-diagnosis-</u> <u>staging/staging.html</u>
- 2. <u>www.cancer.org/cancer/types/malignant-mesothelioma/about/malignant-mesothelioma.html</u>
- 3. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinicaltrials.html
- 4. www.cancer.org/cancer/types/malignant-mesothelioma/about/new-research.html
- 5. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/pain.html</u>
- 7. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 8. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html

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Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

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