

# Treating Gastrointestinal Carcinoid Tumors

If you've been diagnosed with a gastrointestinal (GI) carcinoid tumor, 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.

# Which treatments are used for GI Carcinoid Tumors?

The main types of treatment for GI carcinoid tumors are:

- Surgery for Gastrointestinal Carcinoid Tumors
- Chemotherapy and Other Drugs for Gastrointestinal Carcinoid Tumors
- Radiation Therapy for Gastrointestinal Carcinoid Tumors

#### **Common treatment approaches**

In some cases, doctors may recommend combining two or more types of treatment. Some of the factors that might influence your treatment options are:

- What organ the tumor started in
- The tumor size and location
- Whether it has spread to lymph nodes, liver, bones, or other organs
- Whether you have any other serious medical conditions
- Whether the tumor is causing bothersome symptoms (including symptoms of <u>carcinoid syndrome</u>)
- Treatment of Gastrointestinal Carcinoid Tumors, by Extent of Disease

#### Who treats GI carcinoid tumors?

Based on your treatment options, you might have different types of doctors on your treatment team, including:

- A surgical oncologist: a doctor who treats cancer with surgery
- A **medical oncologist**: a doctor who treats cancer with medicines
- A radiation oncologist: a doctor who treats cancer with radiation therapy
- A **gastroenterologist**: a doctor who specializes in treatment of diseases of the gastrointestinal (digestive) system
- An **endocrinologist:** a doctor who specializes in the diagnosis and treatment of diseases related to hormones

You might have many other specialists on your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, nutrition specialists, social workers, rehabilitation specialists, psychologists, and other health professionals.

Health Professionals Associated with Cancer Care

#### Making treatment decisions

It's important to discuss and understand all your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs.

Take your time and think about all your options when you make this important decision. If time allows, it's often a good idea to get a second opinion. A second opinion may give you more information and help you feel more confident about the treatment plan you choose.

It's also very important to ask questions if you're not sure about something.

- Questions to Ask About Gastrointestinal Carcinoid Tumors
- Seeking a Second Opinion

#### 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 standard 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 they 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 to help you get through treatment. Options include rides to treatment, lodging, and more. Call us at 1-800-227-2345 and speak with one of our caring, 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 before 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.

# More in Gastrointestinal Carcinoid Tumors

- <u>About Gastrointestinal Carcinoid Tumors</u>
- <u>Causes, Risk Factors, and Prevention</u>
- Early Detection, Diagnosis, and Staging
- Treatment
- <u>After Treatment</u>

# Surgery for Gastrointestinal Carcinoid Tumors

- Surgery and other procedures for carcinoid tumors that have spread to the liver
- More information about Surgery

Many gastrointestinal (GI) carcinoid) tumors can be cured by surgery alone. The type of operation will depend on a number of factors, including the size and location of the tumor, whether the person has any other serious diseases, and whether the tumor is causing the carcinoid syndrome.

Surgeons often try to cure localized carcinoid tumors by removing them completely, which is usually successful.

The options for GI carcinoid tumors that have spread to nearby tissues or to distant parts of the body are more complex. Because most carcinoid tumors grow slowly and some do not cause any symptoms, completely removing all metastatic carcinoid tumors may not always be needed. But in some patients, surgery to remove all visible cancer is the best option. This is particularly true if removing most of the cancer will reduce the level of hormone-like substances causing symptoms.

Several types of operations can be used to treat GI carcinoid tumors. Some of these remove the primary tumor (where the cancer started), while others remove or destroy cancer that has spread (metastasized) to other organs.

# Endoscopic mucosal resection

In this procedure, the cancer is removed through an endoscope. This is most often used to treat small carcinoid tumors of the stomach and duodenum (the first part of the small intestine) and it also can be used to remove small carcinoid tumors of the rectum.

#### Local excision

This operation removes the primary tumor and some normal tissue around it. The edges of the defect are then sewn together. This usually doesn't cause any prolonged problems with eating or bowel movements. This operation may be done for small carcinoid tumors (no larger than 2 cm, or a little less than an inch).

Carcinoid tumors are sometimes removed during an operation being done for some

other reason. This often happens with carcinoid tumors of the appendix. When the appendix is removed (for some other reason), it is examined after surgery, and sometimes a carcinoid tumor is found. Most doctors believe that if the tumor is small — 2 cm or less — removing the appendix (appendectomy) is curative and no other surgery is needed. If the tumor is larger than 2 cm, more surgery may be needed.

Rectal carcinoid tumors may be taken out through the anus, without cutting the skin. Other GI carcinoid tumors can sometimes be locally excised through an endoscope but usually it is done through an incision (cut) in the skin.

#### More extensive surgeries

A larger incision (cut) is needed to remove a larger tumor along with nearby tissues. This also gives the surgeon the chance to see if the tumor has grown into other tissues in the abdomen (belly). If it has, the surgeon may be able to remove the areas of cancer spread.

**Partial gastrectomy:** In this operation, part of the stomach is removed. If the upper part is removed, sometimes part of the esophagus is removed as well. If the lower part of the stomach is removed, sometimes the first part of the small intestine (the duodenum) is also taken. Nearby lymph nodes are also removed. This operation is also known as a **subtotal gastrectomy**.

**Small bowel (intestine) resection:** This is an operation to remove a piece of the small intestine (also called the small bowel). When it is used to treat a small bowel carcinoid, this surgery includes removing the tumor and some of the small bowel around it (called a **wide margin resection**). It will also remove nearby (regional) lymph nodes and the supporting connective tissue (called the mesentery) that contains lymph nodes and vessels that carry blood to and from the intestine. Tumors in the terminal ileum (the last part of the small bowel) may require removing the right side of the colon (**hemicolectomy**).

**Pancreaticoduodenectomy (Whipple procedure)**: This operation is most often used to treat pancreatic cancer, but it is also used to treat cancers of the duodenum (the first part of the small intestine). It removes the duodenum, part of the pancreas, nearby lymph nodes and part of the stomach. The gallbladder and part of the common bile duct are removed and the remaining bile duct is attached to the small intestine so that bile from the liver can continue to enter the small intestine. This is a complex operation that requires a lot of skill and experience. It carries a relatively high risk of complications that could even be fatal.

Segmental colon resection or hemicolectomy: This operation removes between one-

third and one-half of the colon, as well as the nearby layers of tissue that hold and connect the intestines ( the mesentery), which includes blood vessels and lymph nodes.

**Low anterior resection:** This operation can be used for some tumors in the upper part of the rectum. It removes some of the rectum and the remaining ends are sewn together. This does not have much effect on digestive function.

**Abdominoperineal (AP) resection:**This surgery is done for large or very invasive cancers in the lower part of the rectum. It removes the anus, rectum, and lower part of the colon. After this operation, the end of the colon is connected to an opening on the skin on the abdomen (called a colostomy). A bag attached over this opening collects stool (feces) as it leaves the body. (For more information, see <u>Colostomy Guide</u><sup>1</sup>).

# Surgery and other procedures for carcinoid tumors that have spread to the liver

If the cancer spreads to the liver, treating the tumors in the liver may help with symptoms. When there are only 1 or 2 tumors in the liver, they may be removed with surgery. If there are more than just a few liver tumors (or if a person is too sick for surgery), othertechniques may be used.

#### Liver resection

In this operation, one or more pieces of the liver that contain areas of cancer are removed. If it isn't possible to remove all areas of cancer, surgery may still be done to remove as much tumor as possible to help reduce symptoms of carcinoid syndrome. This is sometimes called cytoreductive surgery. Removing liver metastases may help some people with carcinoid tumors live longer, but most people who have this surgery will eventually develop new liver metastases.

# Ablation

Ablation techniques destroy tumors without removing them. They are generally best for tumors no more than about 2 cm (a little less than an inch) across.

**Radiofrequency ablation** (RFA) uses high-energy radio waves for treatment. A thin, needle-like probe is placed through the skin and into the tumor. Placement of the probe is guided by ultrasound or CT scans. The tip of the probe releases a high-frequency current that heats the tumor and destroys the cancer cells.

Ethanol (alcohol) ablation (also known as percutaneous ethanol injection) kills the

cancer cells by injecting concentrated alcohol directly into the tumor. This is usually done through the skin using a needle guided by ultrasound or CT scans.

#### **Microwave thermotherapy**

Uses microwaves to heat and destroy the cancer cells.

#### Cryosurgery (cryotherapy)

Cryotherapy destroys a tumor by freezing it with a metal probe. The probe is guided through the skin and into the tumor using ultrasound. Then very cold gasses are passed through the probe to freeze the tumor, killing the cancer cells. This method may be used to treat larger tumors compared to the other ablation techniques, but it sometimes requires general anesthesia (where you are asleep).

#### Embolization

**Intra-arterial therapy and chemoembolization (also known as transarterial embolization or TAE):** This is another option for tumors that can't be removed completely. It can be used for larger tumors (up to about 5 cm or 2 inches across). This technique reduces the blood flow to the cancer cells by blocking the branch of the <u>hepatic artery</u><sup>2</sup> feeding the area of the liver containing the tumor. Blood flow is blocked (or reduced) by injecting materials that plug up the artery. Most of the healthy liver cells will not be affected because they get their blood supply from a different blood vessel, the portal vein.

In this procedure a thin, flexible catheter is put into an artery in the inner thigh and threaded up into the liver. A dye is then injected into the bloodstream to allow the doctor to monitor the path of the catheter via angiography, a special type of x-ray. Once the catheter is in place, small particles are injected into the artery to plug it up.

#### Chemoembolization (also known as trans-arterial chemoembolization or TACE):

This procedure combines embolization with chemotherapy. Most often, this is done by using tiny beads that release a chemotherapy drug during the embolization. TACE can also be done by giving chemotherapy through a thin catheter directly into the artery, then plugging up the artery.

**Radioembolization:** In the United States, this is done by injecting small radioactive beads into the hepatic artery. The beads travel to the tumor and give off small amounts of radiation only at the tumor sites.

# More information about Surgery

For more general information about surgery as a treatment for cancer, see  $\underline{Cancer}$ <u>Surgery</u><sup>3</sup>.

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

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-</u> <u>types/surgery/ostomies/colostomy.html</u>
- 2. www.cancer.org/cancer/types/liver-cancer/treating/chemotherapy.html
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html</u>
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html
- 5. <u>www.cancer.gov/types/gi-carcinoid-tumors/hp/gi-carcinoid-treatment-pdq#section/\_21</u>
- 6. www.nccn.org/professionals/physician\_gls/pdf/neuroendocrine.pdf
- 7. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/references.html</u>

# References

National Cancer Institute Physician Data Query (PDQ). Gastrointestinal Carcinoid Tumors Treatment (PDQ®)–Health Professional Version. 2018. Accessed at

https://www.cancer.gov/types/gi-carcinoid-tumors/hp/gi-carcinoid-treatmentpdq#section/\_21<sup>5</sup> on July 25, 2018.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2018. Accessed at

https://www.nccn.org/professionals/physician\_gls/pdf/neuroendocrine.pdf<sup>6</sup> on July 29, 2018.

Norton JA and Kunz PL. Carcinoid) Tumors and the Carcinoid Syndrome. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015:1218–1226.

# See all references for Gastrointestinal Carcinoid Tumor

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# Chemotherapy and Other Drugs for Gastrointestinal Carcinoid Tumors

- Possible side effects of chemotherapy
- Other drugs used for treating gastrointestinal carcinoid tumors
- Targeted drugs
- Interferons

Chemotherapy (chemo) uses anti-cancer drugs that are injected into a vein or a muscle or taken by mouth to kill cancer cells. These drugs enter the blood and reach almost all areas of the body, making this treatment useful for some types of cancers that have spread.

Unfortunately, gastrointestinal (GI) carcinoid tumors often do not respond well to chemo. Because of this, chemo generally is used only for tumors that have spread to other organs, are causing severe symptoms, have not responded to other medicines or are high grade (grade 3).

Some of the chemo drugs used to treat GI carcinoid tumors include:

- Capecitabine (Xeloda)
- 5-fluorouracil (5-FU)
- Doxorubicin (Adriamycin)
- Etoposide (VP-16)
- Dacarbazine (DTIC)
- Streptozocin
- Temozolomide
- Oxaliplatin

Some tumors, especially high-grade tumors, may be treated with more than one drug. For these, combinations of 5-FU plus streptozocin, 5-FU plus doxorubicin or oxaliplatin plus capecitabine may be used.

Doctors 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, and initial treatment is typically 4 to 6 cycles.

# Possible side effects of chemotherapy

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

The <u>side effects</u><sup>1</sup> of chemo depend on the type and dose of drugs given and the length of time they are taken. Common side effects can include:

- Nausea and vomiting<sup>2</sup>
- Loss of appetite
- Hair loss
- Mouth sores
- Diarrhea or constipation
- Increased chance of infections<sup>3</sup> (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets
- <u>Fatigue</u><sup>4</sup>(from having too few red blood cells)

Most side effects go away a short time after treatment is finished. Often medicines can help prevent or minimize many of the side effects. For example, your doctor can prescribe drugs to help prevent or reduce nausea and vomiting.

You should tell your medical team about any side effects or changes you notice while getting chemotherapy, so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced or treatment may need to be delayed or stopped to keep the effects from worsening.

For more information on chemo, see <u>Chemotherapy</u><sup>5</sup>.

# Other drugs used for treating gastrointestinal carcinoid tumors

For people with metastatic GI carcinoid tumors, several medicines can help control symptoms and tumor growth.

#### Somatostatin analogs

These drugs are related to somatostatin, a natural hormone that seems to help slow the growth of neuroendocrine cells. They are especially useful in people who have <u>carcinoid</u> <u>syndrome</u><sup>6</sup>(facial flushing, diarrhea, wheezing, rapid heart rate) and in people whose tumors show up on a <u>somatostatin receptor scintigraphy</u><sup>7</sup> (SRS) scan or <u>gallium-68</u> <u>Dotatate scans</u><sup>8</sup>.

**Octreotide:** This drug is helpful in treating the symptoms of carcinoid syndrome. Sometimes octreotide can temporarily shrink carcinoid tumors, but it does not cure them.

The original version of octreotide (Sandostatin<sup>®</sup>) is injected under the skin (subcutaneously) at least twice daily. Some people learn to give this injection themselves at home. A long-acting version of the drug (Sandostatin LAR<sup>®</sup>) is injected into a muscle once a month by your doctor or nurse. Depending on the severity of symptoms, some people are given injections every day when first starting treatment. Once the doctor finds the correct dose, the longer-acting monthly injection may then be used.

Side effects can include pain or burning at the injection site, stomach cramps, nausea, vomiting, headaches, dizziness, and fatigue.

**Lanreotide(Somatuline<sup>®</sup>)**: This drug is similar to octreotide. It is injected under the skin once a month. It may be given by your doctor or nurse, or you may learn how to give the injection at home. Side effects are similar to those of octreotide, although pain at the injection site is less common.

**Telotristat (Xermelo<sup>™</sup>):** This drug is used along with a somatostatin analog (octreotide or lanreotide) to help control carcinoid syndrome diarrhea. It is given by mouth as a pill and common side effects can include fever, poor appetite, headache, nausea, and swelling of the hands or feet

# **Targeted drugs**

<u>Anti-cancer drugs that work differently</u><sup>9</sup> from standard chemotherapy drugs have been

developed for some types of cancer. These drugs target specific parts of cancer cells. They are sometimes helpful when chemotherapy is not. They often have different side effects.

The targeted drug, everolimus (Afinitor<sup>®</sup>), has been shown to help treat advanced GI carcinoid tumors. It can be used with or without somatostatin drugs, such as octreotide. Common side effects include diarrhea, fatigue, rash, mouth sores and swelling of the legs or arms.

# Interferons

Interferons are natural substances that normally activate the body's immune system. They also slow the growth of some tumor cells. Interferon-alfa is sometimes helpful in shrinking or slowing the growth of metastatic GI carcinoid tumors and improving symptoms of carcinoid syndrome. Often, the drug's usefulness is limited by its flu-like side effects, which may be severe. The drug is given by injection.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 5. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 6. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-</u> staging/signs-symptoms.html
- 7. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-</u> staging/how-diagnosed.html
- 8. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-</u> <u>staging/how-diagnosed.html</u>
- 9. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 10. www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/references.html

# References

Chan JA, Kulke M, Clancy TE. Metastatic gastroenteropancreatic neuroendocrine tumors: Local options to control tumor growth and symptoms of hormone

hypersecretion. UpToDate website. https://www.uptodate.com/contents/metastaticgastroenteropancreatic-neuroendocrine-tumors-local-options-to-control-tumor-growthand-symptoms-of-hormone-hypersecretion? Updated Dec. 11, 2017. Accessed August 5, 2018.

Cho CS, Lubner SJ, Kavanagh BD. Chapter 125: Metastatic Cancer to the Liver. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10<sup>th</sup> ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2018. Accessed at https://www.nccn.org/professionals/physician\_gls/pdf/neuroendocrine.pdf on August 5, 2018.

Pandit S, Bhusal K. Carcinoid Syndrome. [Updated 2017 Oct 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448096/ Accessed August 5, 2018.

Pavel M, Gross DJ, Benavent M, et al. Telotristat ethyl in carcinoid syndrome: safety and efficacy in the TELECAST phase 3 trial. *Endocr Relat Cancer*. 2018 Mar;25(3):309-322. doi: 10.1530/ERC-17-0455. Epub 2018 Jan 12.

Yao JC, Fazio N, Singh S, et al. Everolimus for the treatment of advanced, nonfunctional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): A randomised, placebo-controlled, phase 3 study. *Lancet.* 2016;387: 968-77.

See all references for Gastrointestinal Carcinoid Tumor

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# Radiation Therapy for Gastrointestinal Carcinoid Tumors

- External beam radiation therapy (EBRT)
- Procedures using radioactive drugs
- More information about radiation therapy

Radiation therapy is the use of high-energy rays (such as x-rays) or radioactive particles to kill cancer cells.

Although surgery is the main treatment for most carcinoid tumors, radiation therapy may be an option for those who can't have surgery for some reason. It may also be given after surgery in some cases if there's a chance some of the tumor was not removed. Radiation therapy can also be used to help relieve symptoms such as pain if the cancer has spread to the bones or other areas.

# External beam radiation therapy (EBRT)

External beam radiation therapy uses a machine to deliver a beam of radiation to a specific part of the body. This type of radiation is used most often to treat cancer.

# Side effects of gastrointestinal (GI) radiation therapy

The main side effects of GI radiation therapy are:

- Tiredness (fatigue)
- Nausea and vomiting
- Diarrhea (if the belly or pelvis is treated)
- Skin changes, which can range from mild redness to blistering and peeling
- Hair loss in the area being treated

# Procedures using radioactive drugs

#### Radioembolization

This technique combines embolization with radiation therapy and is used to treat liver metastases.

Embolization is a procedure that injects substances to try to block or reduce the blood flow to cancer cells in the liver. The liver is unusual in that it has 2 blood supplies. Most normal liver cells are fed by the portal vein, whereas cancer cells in the liver are usually fed by the <u>hepatic artery</u><sup>1</sup>. Blocking the branch of the hepatic artery feeding the tumor helps kill off the cancer cells, but it leaves most of the healthy liver cells unharmed because they get their blood supply from the portal vein.

In this procedure, a catheter (a thin, flexible tube) is put into an artery through a small cut in the inner thigh and eased up into the hepatic artery in the liver. A dye is injected into the blood at the same time to allow the doctor to monitor the path of the catheter via angiography, a special type of x-ray. Once the catheter is in place, small particles called microspheres are injected into the artery to plug it up.

In radioembolization, microspheres (small beads) that are attached to a radioactive element called **yttrium-90 (or 90Y)** are used. After they are injected, the beads travel in the liver blood vessels until they get stuck in small blood vessels near the tumor. There they give off radioactivity for a short while, killing nearby tumor cells. The radiation travels a very short distance, so its effects are limited mainly to the tumor.

# Peptide receptor radionuclide therapy (PRRT)

In this form of radiation therapy, a drug is linked to a radioactive element. The drug travels throughout the body, attaches to the cancer cells, and gives off radiation to kill them. It is given through a vein and not directly into the liver like radioembolization.

One option is to use somatostatin analog drugs like octreotide or lanreotide linked with a radioactive form of the element yttrium-90. Another option uses a different radioactive element, called lutetium (Lu-177), that is carried to the cancer cells by dotatate where it attaches to carcinoid tumor cells. These injectable therapies let doctors deliver high doses of radiation directly to the tumors.

For adults and pediatric patients 12 years and older with somatostatin (a type of hormone) receptor-positive GI carcinoid tumors, a radioactive drug, called Lutathera (lutetium Lu- 177 dotatate), can be used for treatment. Lu-177 dotatate,a <u>radiopharmaceutical</u><sup>2</sup>, works by attaching to the somatostatin receptor (protein), which is part of the cancer cell, allowing radiation to enter the cell and cause damage. If you are taking octreotide or lanreotide, you will most likely be asked to stop taking these medicines before Lu-177 dotatate is given.

Common side effects of Lu-177 dotatate include low levels of white blood cells, high levels of enzymes in certain organs, nausea and vomiting, high levels of blood sugar, and low levels of potassium in the blood.

Serious side effects of Lu-177 dotatate include low levels of blood cells, development of certain blood or bone marrow cancers, kidney damage, liver damage, abnormal levels

of hormones in the body, and infertility. Women who are pregnant or might become pregnant should be advised that Lu-177 dotatate can cause harm to a developing fetus.

Lu-177 dotatate is given intravenously and does expose those taking it and possibly others around them to radiation. Family members should know how to protect themselves<sup>3</sup> from being exposed to the radiation.

# More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u><sup>4</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>5</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/liver-cancer/treating/chemotherapy.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/systemic-radiation-therapy.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/systemic-radiation-therapy.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html</u>
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html
- 6. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/references.html</u>

# References

Chan DL, Thompson R, Lam M, et al. External Beam Radiotherapy in the Treatment of Gastroenteropancreatic Neuroendocrine Tumours: A Systematic Review. *Clin Oncol (R Coll Radiol*). 2018 Jul;30(7):400-408. doi: 10.1016/j.clon.2018.03.006. Epub 2018 Mar 31.

Cives, M. & Strosberg, J. Radionuclide Therapy for Neuroendocrine Tumors. *Curr Oncol Rep.* 2017: 19 (9). https://doi.org/10.1007/s11912-017-0567-8

Imhof A, Brunner P, Marincek N, et al. Response, survival, and long-term toxicity after therapy with the radiolabeled somatostatin analogue [90Y-DOTA]-TOC in metastasized neuroendocrine cancers. *J Clin Oncol.* 2011; 29(17):2416–23. doi:10.1200/JCO.2010.33.7873.

Lutetium Lu 177 Dotatate Approved by FDA. *Cancer Discov.* 2018; 8 (4). DOI: 10.1158/2159-8290.CD-NB2018-021.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2018. Accessed at https://www.nccn.org/professionals/physician\_gls/pdf/neuroendocrine.pdf on August 5, 2018.

Norton JA and Kunz PL. Carcinoid) Tumors and the Carcinoid Syndrome. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015:1218–1226.

Schneider DF, Mazeh H, Lubner SJ, Jaume JC, Chen H. Cancer of the Endocrine System. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology.* 5th ed. Philadelphia, Pa: Elsevier; 2014:1112-1142.

Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 Trial of <sup>177</sup>Lu-Dotatate for Midgut Neuroendocrine Tumors. *N Engl J Med*. 2017;376(2):125-135. doi:10.1056/NEJMoa1607427.

See all references for Gastrointestinal Carcinoid Tumor

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# Treatment of Gastrointestinal Carcinoid Tumors, by Extent of Disease

- Localized GI carcinoid tumors
- Regional spread
- Distant spread
- Recurrent carcinoid tumors
- Neuroendocrine carcinomas
- Carcinoid heart disease

Treatment of GI carcinoid tumors is based mostly on their size or how far they have grown into the wall of the organ where they started, as well as if they have spread.

# Localized GI carcinoid tumors

A tumor is localized when it has not spread outside the organ where it started.

# Stomach

Carcinoid) tumors of the stomach are generally grouped by:

- The level of a hormone called gastrin and
- The amount of acid in the stomach (measured before surgery).

The levels of these substances determine the type of stomach carcinoid tumor.

**Type 1:** Patients with this type have high gastrin levels but low levels of stomach acid. These carcinoid tumors tend to be small, but there may be many of them. The tumors don't tend to grow into the deeper layers of the stomach or spread to other organs or tissues, and are often treated by removing them completely through an endoscope. The other option is to watch the tumors closely (by endoscopy), and only removing them if they start growing.

**Type 2:** Patients with this type have high gastrin levels and high stomach acid levels. Like type 1, these tumors are often small and there may be more than one at a time. Type 2 tumors also don't tend to grow into deeper layers of the stomach or spread to other organs.

Small tumors can be watched closely without treatment, removed with endoscopy, or treated with a medicine like octreotide or lanreotide that will lower levels of both gastrin and stomach acid. High doses of proton pump inhibitors, such as omeprazole or lansoprazole, may also be used to control the stomach acid. For tumors larger than 2 cm (slightly less than an inch), just watching the tumor closely isn't usually an option. These tumors need to be removed, either through an endoscope or in a regular operation through an incision in the abdomen that removes the tumor and some surrounding stomach tissue.

**Type 3:** Patients with type 3 tumors have normal levels of gastrin and stomach acid. There is usually only one tumor, and the tumor tends to grow into deeper layers of the

stomach or even spread to nearby lymph nodes or other organs (like the liver). If the tumor is small, endoscopic surgery may still be an option. More, often, though, more extensive surgery with a partial gastrectomy (a piece of the stomach is removed) and removal of nearby lymph nodes is needed.

#### **Small intestine**

Some small tumors in the duodenum (the first part of the small intestine) can often be removed through the endoscope (endoscopic resection). Depending on the size of the tumor and whether it is growing into nearby tissues, other options include surgery to remove the tumor (local excision), removing all or part of the duodenum with nearby lymph nodes, and removing the duodenum and part of the pancreas (a pancreatoduodenectomy).

For tumors in other parts of the small intestine, treatment is either local excision for small tumors or small bowel resection (removal of a piece of intestine as well as some surrounding blood vessels and lymph nodes) for larger tumors.

# Large intestine (other than appendix and rectum)

The usual treatment is hemicolectomy (removal of a section of colon along with nearby lymph nodes and blood vessels). Because many patients have more than one carcinoid tumor, the surgeon will often check the rest of the colon for other tumors during surgery. For very small tumors, sometimes the tumor can be removed without surgery using a colonoscope.

# Appendix

Most often, an appendectomy (surgical removal of the appendix) is the only treatment needed for carcinoid tumors that are 2 cm (a little less than an inch) across or smaller. Still, other factors, such as the way the tumor cells look, the patient's age, general health, and the patient's degree of worry about the possibility of the cancer coming back, might also be used to determine whether more treatment is needed.

Tumors larger than 2 cm are more likely to have already spread to nearby tissues and lymph nodes, so more extensive surgery is usually recommended. This means removal of about a third of the colon next to the appendix (a hemicolectomy), along with nearby blood vessels and lymph nodes. This procedure might not be recommended for people who are older or have other serious health problems (especially if these problems make surgery more risky), because the benefit might not outweigh the risks.

#### Rectum

Most rectal carcinoid tumors that are smaller than 1 cm (slightly less than half an inch) can be removed by an endoscope or local excision through the anus .

The best approach for rectal carcinoid tumors between 1 and 2 cm, depends on how deeply the tumor has grown into the wall of the rectum, as well as if it has invaded the nearby lymph nodes. Doctors can check for this before surgery by using an endoscopic ultrasound. If the tumor has grown into the thick muscle layer of the rectum (the muscularis propria) or deeper or if local lymph nodes have tumor cells, it needs to be treated the same as a larger tumor. If not, it may still be able to be removed by endoscope or local excision through the anus.

Tumors larger than 2 cm (and those that have grown deep into the wall of the rectum) have a higher risk of growing and spreading, so they are removed by the same operations used for adenocarcinomas (the usual type of rectal cancer). This operation is a low anterior resection if the tumor is in the upper part of the rectum. If the lower part is involved, abdominoperineal (AP) resection and <u>colostomy</u><sup>1</sup> are used.

# **Regional spread**

Regional spread means that the cancer has either spread to nearby lymph nodes or it has grown through the wall of the organ where it started and has invaded nearby tissues such as fat, ligaments, and muscle.

If possible, the primary (main) tumor and any areas of cancer spread should all be removed by surgery. Nearby lymph nodes should be removed and checked for signs of cancer spread. This provides the best chance of cure. If this can't be done, surgery should remove as much cancer as possible without causing severe side effects. Surgery should also be done to relieve symptoms such as intestinal blockage caused by the local growth of the tumor.

If all of the tumor cannot be removed at the time of surgery, treatment with somatostatin drugs, like octreotide or lanreotide, or targeted drugs, like everolimus, can be considered because they may control the remaining cancer.

# **Distant spread**

At this stage, the cancer has spread to other organs such as the liver and a cure is not usually possible. Treatment is not always needed right away, depending on how quickly the tumors are growing. The goal of surgery in this situation is usually to relieve

symptoms and slow the course of the disease. For example, removing or bypassing areas blocked by cancer growth can relieve some symptoms. If distant metastases are not causing symptoms, treatment may not be needed. If the cancer has spread to the liver, even when it isn't causing symptoms, some doctors recommend treatment with octreotide or lanreotide, chemotherapy, ortargeted therapy because it may slow tumor growth.

If carcinoid syndrome is causing bothersome symptoms, treatment options include chemotherapy, targeted therapy, treatment with octreotide or lanreotide, or surgery to remove the metastatic tumors. If metastatic tumors in the liver cannot be removed by surgery without causing severe side effects, ablation or embolization can be used to destroy as much of the tumors as possible. Patients should also be advised to avoid alcoholic drinks, stress, strenuous exercise, spicy foods, and certain medicines that can make the symptoms of carcinoid syndrome worse.

# **Recurrent carcinoid tumors**

When cancer comes back after treatment it is called a recurrence. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). Patients with recurrent carcinoid tumors are treated sometimes with surgery to remove all signs of tumor if possible. This provides the best chance for a good long-term outcome. If surgery is not possible, the treatments used for distant spread may be helpful. For more information, see <u>Understanding Recurrence</u><sup>2</sup>.

# **Neuroendocrine carcinomas**

Gastrointestinal neuroendocrine carcinomas (NECs) are high-grade (grade 3) tumors that grow very quickly. There are also some low- (grade 1) and intermediate-grade (grade 2) carcinoid tumors that act like neuroendocrine carcinomas because they grow fast. These cancers are treated differently from most carcinoid tumors (grade 1 and 2) because they are treated with chemotherapy first.

# Carcinoid heart disease

The substances released into the blood by some carcinoid tumors can damage the heart. Early symptoms are fatigue and shortness of breath. Eventually, patients get fluid in their legs and even their abdomen. The major cause is damage to the valves of the heart. Doctors can usually make the diagnosis by listening to the heart and by an ultrasound of the heart called an echocardiogram.

The main treatment is with a somatostatin analog like octreotide or lanreotide to block the tumor's secretion of the toxic substances. Drugs (diuretics) to get rid of extra fluid can also help. In some instances, heart surgery may be needed to replace the damaged valves.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-</u> <u>types/surgery/ostomies/colostomy.html</u>
- 2. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 3. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/references.html</u>

# References

Kunz PL. Carcinoid and neuroendocrine tumors: building on success. *J Clin Oncol.* 2015;33(16):1855-63. doi: 10.1200/JCO.2014.60.2532.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2018. Accessed at https://www.nccn.org/professionals/physician\_gls/pdf/neuroendocrine.pdf on August 5, 2018.

Oronsky B, Ma PC, Morgensztern D, Carter CA. Nothing But NET: A Review of Neuroendocrine Tumors and Carcinomas. *Neoplasia*. 2017;19(12):991-1002. doi:10.1016/j.neo.2017.09.002.

Singh S, Sivajohanathan D, Asmis T, et al. Systemic therapy in incurable gastroenteropancreatic neuroendocrine tumours: a clinical practice guideline. *Current Oncology*. 2017;24(4):249-255. doi:10.3747/co.24.3634.

See all references for Gastrointestinal Carcinoid Tumor

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