Treating Liver Cancer

team. These doctors may include:

- A **surgical oncologist:** a doctor who treats cancer with surgery.
- A **radiation oncologist:** a doctor who treats cancer with radiation therapy.
  A

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.

Surgery for Liver Cancer

The best option to cure liver cancer is with either surgical resection (removal of the tumor with surgery) or a liver transplant. If all cancer in the liver is completely removed, you will have the best outlook. Small liver cancers may also be cured with other types of treatment such as ablation or radiation.

Partial hepatectomy

Partial hepatectomy is surgery to remove part of the liver. Only people with good liver function who are healthy enough for surgery and who have a single tumor that has not grown into blood vessels can have this operation.

Imaging tests[1], such as CT or MRI with angiography are done first to see if the cancer can be removed completely. Still, sometimes during surgery the cancer is found to be too large or has spread too far to be removed, and the surgery that has been planned cannot be done.

Most patients with liver cancer in the United States also have cirrhosis[2]. In someone with severe cirrhosis, removing even a small amount of liver tissue at the edges of a cancer might not leave enough liver behind to perform important functions.

People with cirrhosis are typically eligible for surgery if there is only one tumor (that has not grown into blood vessels) and they will still have a reasonable amount (at least 30%) of liver function left once the tumor is removed. Doctors often assess this function by assigning a Child-Pugh score (see Liver Cancer Stages[3]), which is a measure of cirrhosis based on certain lab tests and symptoms.

Patients in Child-Pugh class A are most likely to have enough liver function to have surgery. Patients in class B are less likely to be able to have surgery. Surgery is not typically an option for patients in class C.

Possible risks and side effects

Liver resection is a major, serious operation that should only be done by skilled and experienced surgeons. Because people with liver cancer usually have other liver

problems besides the cancer, surgeons have to remove enough of the liver to try to get all of the cancer, but also leave enough behind for the liver to function.

- Bleeding: A lot of blood passes through the liver, and bleeding after surgery is a major concern. Also, the liver normally makes substances that help the blood clot. Damage to the liver (both before the surgery and during the surgery) can add to potential bleeding problems.
- Infection
- Complications from anesthesia
- Blood clots
- Pneumonia
- New liver cancer: Because the remaining liver still has the underlying disease that led to the cancer, sometimes a new liver cancer can develop afterward.

Liver transplant

When it is available, a liver transplant may be the best option for some people with liver cancer. Liver transplants can be an option for those with tumors that cannot be removed with surgery, either because of the location of the tumors or because the liver has too much disease for the patient to tolerate removing part of it. In general, a transplant is

Hyperlinks

1. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html
2. www.cancer.org/cancer/types/liver-cancer/causes-risks-prevention/risk-factors.html
3. www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/staging.html
4. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
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Last Revised: April 1, 2019

Ablation for Liver Cancer

- Radiofrequency ablation (RFA)
- Microwave ablation (MWA)
- Cryoablation (cryotherapy)
- Ethanol (alcohol) ablation
- Side effects of ablation therapy

Ablation is treatment that destroys liver tumors without removing them. These techniques can be used in patients with a few small tumors and when surgery is not a good option (often because of poor health or reduced liver function). They are less likely to cure the cancer than surgery, but they can still be very helpful for some people. These treatments are also sometimes used in patients waiting for a liver transplant.

Ablation is best used for tumors no larger than 3 cm across (a little over an inch). For slignt.

Cryoablation (cryotherapy)

Cryoablation destroys a tumor by freezing it using a thin metal probe. The probe is guided into the tumor and then very cold gasses are passed through the probe to freeze the tumor which causes the cancer cells to die.

Ethanol (alcohol) ablation

This is also known as **percutaneous ethanol injection (PEI)**. In this procedure, concentrated alcohol is injected directly into the tumor to damage cancer cells.

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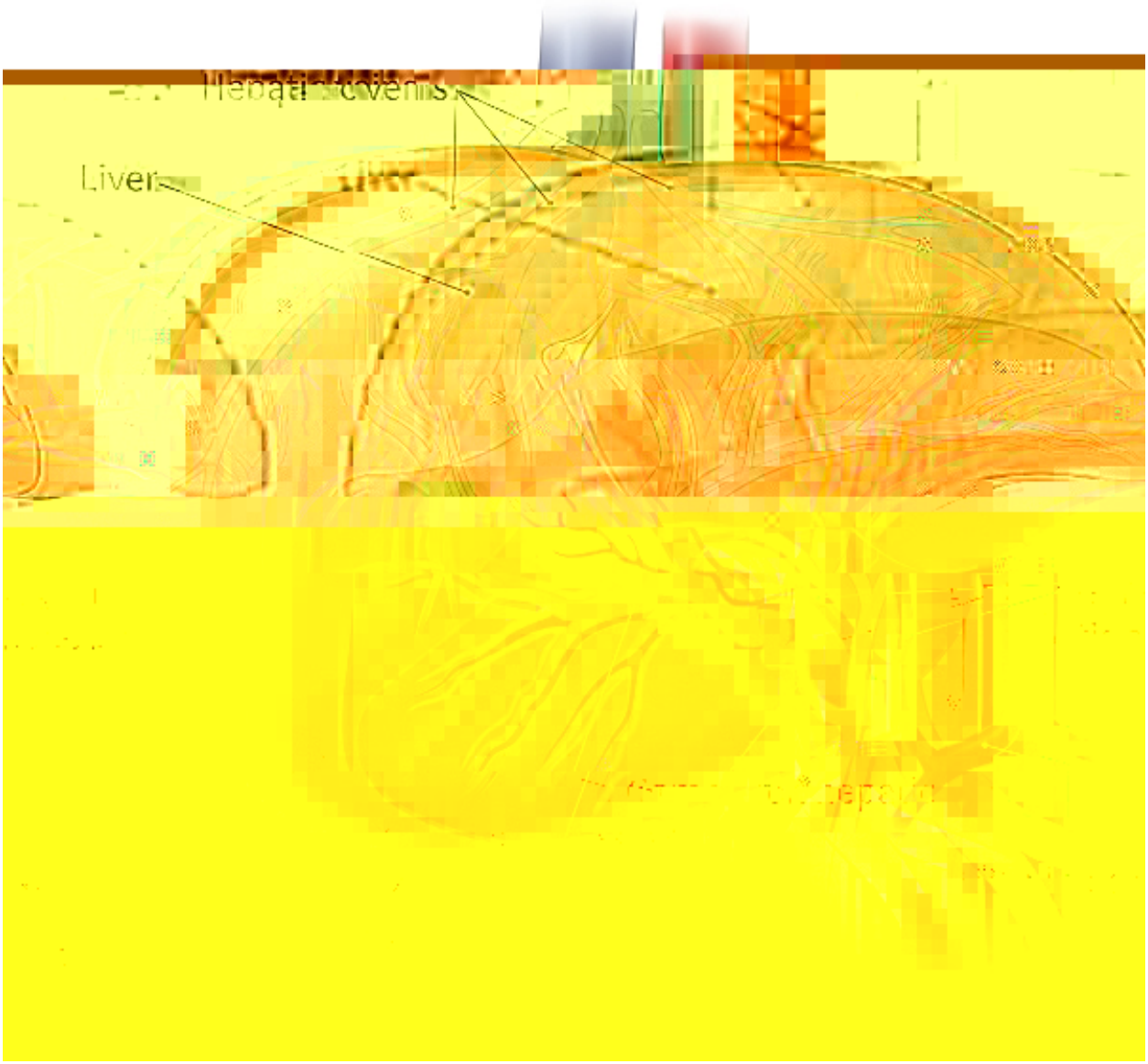
Embolization Therapy for Liver Cancer

Embolization is a procedure that injects substances directly into an artery in the liver to block or reduce the blood flow to a tumor in the liver.

The liver is special in that it has 2 blood supplies. Most normal liver cells are fed by the **portal vein**, whereas a cancer in the liver is mainly fed by the **hepatic artery**. Blocking the part of the hepatic artery that feeds 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.



Embolization isan option for some patients with tumors that cannot be removed by surgery. It can be used for people with tumors that are too large to be treated with ablation (usually larger than 5 cm across) and who also have adequate liver function. It can also be used with ablation. Embolization can reduce some of the blood supply to the normal liver tissue, so it may not be a good option for some patients whose liver has been damaged by diseases such as hepatitis or cirrhosis. It isn't yet clear which type of embolization has a better long-term outcome.

People getting this type of treatment typically do not stay in the hospital overnight.

Trans-arterial embolization (TAE)

During trans-arterial embolization a catheter (a thin, flexible tube) is put into an artery in the inner thigh through a small cut and eased up into the hepatic artery in the liver. A dye is usually injected into the bloodstream to help the doctor watch the path of the catheter. Once the catheter is in place, small particles are injected into the artery to plug it up, blocking oxygen and key nutrients from the tumor.

Trans-arterial chemoembolization (TACE)

Trans-arterial chemoembolization is usually the first type of embolization used for large liver cancers that cannot be treated with surgery or ablation. It combines embolization with chemotherapy (chemo). Most often, this is done by giving chemotherapy through the catheter directly into the artery, then plugging up the artery, so the chemo can stay close to the tumor.

Drug-eluting bead chemoembolization (DEB-TACE)

Drug-eluting bead chemoembolization combines TACE embolization with drug-eluting beads (tiny beads that contain a chemotherapy drug). The procedure is essentially the same as TACE except that the artery is blocked after drug-eluting beads are injected. Because the chemo is physically close to the cancer and because the drug-eluting beads slowly release the chemo, the cancer cells are more likely to be damaged and die. The most common chemo drugs used for TACE or DEB-TACE are mitomycin C, cisplatin, and doxorubicin.

Radioembolization (RE)

Radioembolization combines embolization with radiation therapy. This is done by injecting small beads (called *microspheres*) that have a radioactive isotope (yttrium-90 or Y-90) attached to them into the hepatic artery. Once infused, the beads lodge in the blood vessels near the tumor, where they give off small amounts of radiation to the tumor site for several days. The radiation travels a very short distance, so its effects are limited mainly to the tumor.

Possible side effects of embolization

Possible complications after embolization include:

- Abdominal pain
- Fever

- Nausea
- Infection in the liver
- Blood clots in the main blood vessels of the liver

Sometimes, it can take 4-6 weeks to fully recover from the procedure. Because healthy liver tissue can be affected, there is a risk that liver function will get worse after embolization. This risk is higher if a large branch of the hepatic artery is embolized. Serious complications are not common, but they are possible.

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Radiation Therapy for Liver Cancer

the treatment to avoid damaging normal liver tissue as much as possible. Newer radiation techniques, such as **stereotactic body radiation therapy (SBRT)**, help doctors target liver tumors while reducing the radiation to nearby healthy tissues. This makes it more effective and reduces side effects. SBRT allows treatment to be completed in a short-time compared to EBRT. It uses very focused beams of high-dose radiation given on one or a few days. Beams are aimed at the tumor from many different angles. To focus the radiation precisely, the person is put in a specially designed body frame for each treatment. This type of radiation may be used in people with small cancers who are waiting for a liver transplant.

Radioembolization

As mentioned in Embolization Therapy for Liver Cancer, tumors in the liver can be treated by injecting small radioactive beads into the hepatic artery. The beads then lodge in the liver near the tumor and give off small amounts of radiation that travel only a short distance.

Possible side effects of radiation therapy for liver cancer

Some of the more common side effects of radiation therapy include:

- Skin changes in areas getting radiation, ranging from redness to blistering and peeling
- Nausea and vomiting
- Fatigue
- Diarrhea
- Loss of appetite

These effects typically go away within a few weeks after treatment ends.

A more serious side effect of radiation therapy to the liver is **radiation-induced liver disease (RILD)**. It commonly happens 3 to 4 months after treatment and usually only lasts a set time, but can be fatal in some instances. Signs and symptoms seen with RILD can include abnormal blood liver tests, an enlarged liver and spleen, ascites (fluid build up in the abdomen), and jaundice. Ask your doctor what side effects to expect and how to prevent or relieve them.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy[2].

Targeted Drug Therapy for Liver Cancer

As researchers learn more about the changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. Targeted drugs work differently from standard chemotherapy drugs (which are described in Chemotherapy for Liver Cancer) and often have different side effects.

Like chemotherapy, these drugs enter the bloodstream and reach almost all areas of the body, which makes them potentially useful against cancers that have spread to distant parts of the body. Because standard chemo is not very effective in most patients with liver cancer, doctors are focusing more on using targeted therapies.

Kinase inhibitors

Kinases are proteins on or near the surface of a cell that carry important signals to the cell's control center. Many of the targeted drugs used to treat liver cancer are **kinase inhibitors**. These drugs block several kinase proteins, which normally help tumor cells grow in one of two ways:

- Some kinases help tumor cells grow directly.
- Some kinases help tumors form the new blood vessels they need in order to get bigger (a process called **angiogenesis**).

Blocking these proteins can often help stop the growth of the cancer.

Sorafenib (Nexavar) and lenvatinib (Lenvima)

One of these drugs can be used as the first treatment for liver cancer if it cannot be treated by surgery or if it has spread to other organs.

Sorafenib is a pill taken twice daily. Lenvatinib is a pill that is taken once a day.

Sorafenib may work better in people with liver cancer caused by hepatitis C.

Regorafenib (Stivarga) and cabozantinib (Cabometyx)

These drugs can be used to treat advanced liver cancer, typically if other treatments are no longer helpful.

Regorafenib is a pill, typically taken once a day for 3 weeks, followed by a week off. Cabozantinib is a pill taken once a day.

Side effects of kinase inhibitors

Common side effects of these drugs can include fatigue, loss of appetite, hand-foot syndrome (redness and irritation of the hands and feet), high blood pressure, weight loss, diarrhea, and abdominal (belly) pain.

Less common but more serious side effects can include problems with blood flow to the heart, bleeding, abnormal thyroid tests, and perforations (holes) in the stomach or intestines.

Monoclonal antibodies

Monoclonal antibodies are man-made versions of immune system proteins (antibodies) that are designed to attach to a specific target. The monoclonal antibodies used to treat

Side effects of angiogenesis inhibitors

Common side effects of these drugs can include:

- High blood pressure
- Tiredness (fatigue)
- Bleeding
- Low white blood cell counts (with increased risk of infections)
- Headaches
- Mouth sores
- Loss of appetite
- Diarrhea

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Immunotherapy for Liver Cancer

Immunotherapy is the use of medicines that help a person’s own immune system find and destroy cancer cells. It can be used to treat some people with liver cancer.

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” – proteins on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. Newer drugs that target these checkpoints hold a lot of promise as liver cancer treatments.

PD-1 and PD-L1 inhibitors

PD-1 is a checkpoint protein on immune cells called *T cells*. When PD-1 attaches to PD-L1, a protein on other cells in the body, it acts as a type of “off switch” that basically tells the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1, which helps them hide from an immune attack. Drugs that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells.

Atezolizumab (Tecentriq) and **durvalumab (Imfinzi)** target the PD-L1 protein. Blocking this protein can help boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

Atezolizumab can be used along with the targeted drug bevacizumab (Avastin) as the first treatment for liver cancer that cannot be treated by surgery or that has spread to other organs.

Durvalumab can be used with another immunotherapy drug tremelimumab (Imjudo) as the first treatment for liver cancer that cannot be removed with surgery.

These drugs are given as an infusion into a vein (IV), typically once every 2, 3, or 4 weeks. Atezolizumab (as **Tecentriq Hybreza**) can also be given as an injection under the skin (subcutaneously) over several minutes, typically once every 3 weeks.

Pembrolizumab (Keytruda) and **nivolumab (Opdivo)** are drugs that target PD-1, which can help boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

These drugs can be used in people with advanced liver cancer who have previously been treated (such as with the

Ipilimumab (Yervoy) and **tremelimumab (Imjudo)** are other types of drugs that boost the immune response, but they have a different target. They block CTLA-4, another protein on T cells that normally helps keep them in check.

Tremelimumab (Imjudo) can be used with another immunotherapy drug durvalumab as the first treatment for liver cancer that cannot be removed with surgery. It is given as an intravenous (IV) infusion once every 4 weeks.

Ipilimumab can be used in combination with nivolumab to treat liver cancer that has previously been treated (such as with the targeted drug sorafenib). This drug is given as an intravenous (IV) infusion, usually once every 3 weeks for 4 treatments.

Possible side effects of checkpoint inhibitors

Side effects of these drugs can include:

- Feeling tired or weak
- Fever
- Cough
- Nausea
- Itching
- Skin rash
- Loss of appetite
- Muscle or joint pain
- Constipation or 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 these drugs.

Autoimmune reactions: These drugs work by basically removing one of the safeguards on the body's immune system. Sometimes the immune system 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, skin, or other organs.

Serious side effects seem to occur more often with ipilimumab than with the PD-1 and

PD-L1 inhibitors.

It's very important to report any new side effects to your health care team promptly. If serious side effects do occur, treatment may need to be stopped and you may get 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 Cancer Immunotherapy[1].

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

Hyperlinks

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

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Chemotherapy for Liver Cancer

Chemotherapy (chemo) is treatment with drugs to destroy cancer cells. Chemo may be an option for people whose liver cancer cannot be treated with surgery, has not responded to local therapies such as ablation or embolization, or when targeted therapy is no longer helpful.

Which chemotherapy drugs are used for liver cancer?

Unfortunately, most chemo drugs do not have a great effect on liver cancer. Recent advances have shown that a combination of drugs may be more helpful than using just a single chemo drug. But even these combinations of drugs shrink only a small number of tumors, and the responses often do not last long. And most studies show systemic chemo has not helped patients live longer.

The most common chemotherapy drugs for treating liver cancer include:

- Gemcitabine (Gemzar)
- Oxaliplatin (Eloxatin)
- Cisplatin
- Doxorubicin (pegylated liposomal doxorubicin)
- 5-fluorouracil (5-FU)

- Capecitabine (Xeloda)
- Mitoxantrone (Novantrone)

Sometimes, combinations of 2 or 3 of these drugs are used. GEMOX (gemcitabine plus oxaliplatin) is one option for people who are fairly healthy and may tolerate more than one drug. 5-FU based chemotherapy, for example with FOLFOX (5-FU, oxaliplatin and leucovorin), is another option for people with bad liver disease.

How is chemotherapy given?

You can get chemotherapy in different ways.

Systemic chemotherapy

Drugs are injected right into a vein (IV) or taken by mouth. These drugs enter the bloodstream and reach almost all areas of the body, possibly making this treatment useful for cancers that have spread to other parts of the body.

For IV chemo, a slightly larger and sturdier catheter is required in the vein system to administer chemo. They are known as central venous catheters[1] (CVCs), central venous access devices (CVADs), or central lines. They are used to put medicines, blood products, nutrients, or fluids right into your blood. They can also be used to take out blood for testing. Many different kinds of CVCs are available. The 2 most common types are the port and the PICC line.

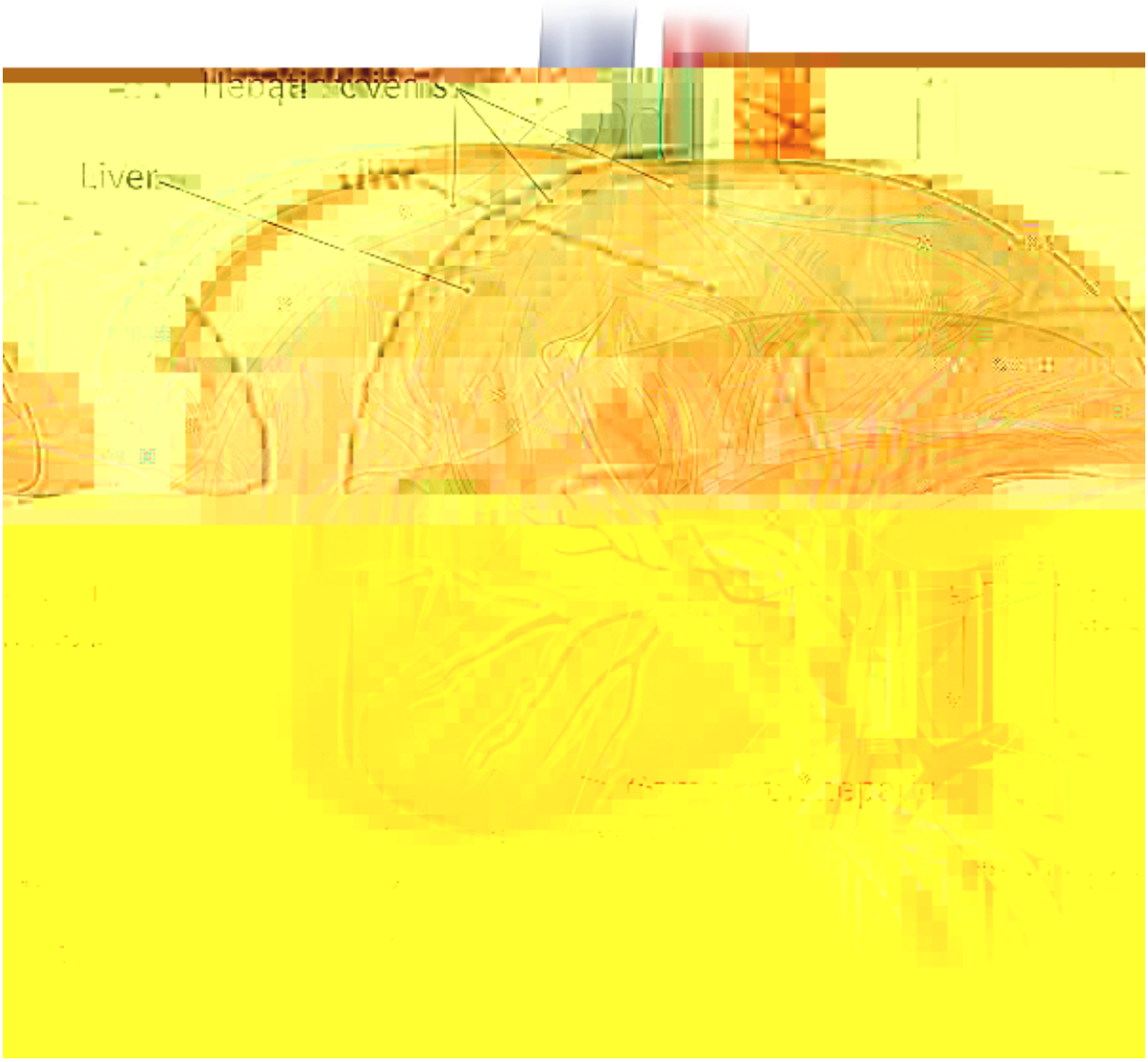
Doctors give chemo in cycles, with each period of treatment followed by a rest period to give you time to recover from the effects of the drugs. Cycles are most often 2 or 3 weeks long. The schedule varies depending on the drugs used. For example, with some drugs, the chemo is given only on the first day of the cycle. With others, it is given for a few days in a row, or once a week. Then, at the end of the cycle, the chemo schedule repeats to start the next cycle.

Treatment for advanced liver cancer is based on how well it is working and what side effects you have.

Regional chemotherapy

Drugs are put right into an artery that leads to the part of the body with the tumor. This focuses the chemo on the cancer cells in that area. It reduces side effects by limiting the amount of drug reaching the rest of the body. Hepatic artery infusion, or chemo given

directly into the hepatic artery, is regional chemotherapy that can be used for liver cancer.



Hepatic artery infusion

Doctors have studied putting chemo drugs directly into the hepatic artery at a constant rate to see if it might be more effective than systemic chemo. This technique is known as hepatic artery infusion (HAI). It is slightly different from chemoembolization because surgery is needed to put an infusion pump under the skin of the abdomen (belly). The pump is attached to a catheter that connects to the hepatic artery. This is done while the patient is under general anesthesia. The chemo is injected with a needle through the

skin into the pump' reservoir and it is released slowly and steadily into the hepatic artery.

The healthy liver cells break down most of the drug before it can reach the rest of the body. This method gets a higher dose of chemo to the tumor than systemic chemo but doesn't increase side effects. The drugs most commonly used for HAI include floxuridine (FUDR), cisplatin, and oxaliplatin.

HAI may be used for people with very large liver cancers that cannot be removed with surgery or cannot be treated entirely with TACE. This technique may not be useful in all patients because it requires surgery to insert the pump and catheter, an operation that many liver cancer patients may not be able to tolerate.

Early studies have found that HAI is often effective in shrinking tumors, but more research is still needed.

Possible side effects of chemotherapy for liver cancer

Chemo drugs attack cells that are dividing quickly, whi518.15F Tfna.227.2345

Along with the possible side effects in the list above, some drugs may have their own specific side effects. Ask your health care team what you can expect.

You should report any side effects you notice while getting chemotherapy to your medical team so that you can be treated promptly. In some cases, the doses of the chemotherapy drugs may need to be reduced or treatment may need to be delayed or stopped to prevent side effects from getting worse.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy[2].

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

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html
2. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
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Treatment of Liver Cancer, by Stage

- Potentially resectable or transplantable liver cancer (stage I and some stage II cancers)
- Unresectable (inoperable) liver cancer that has not spread
- Advanced (metastatic) liver cancer (includes all N1 or M1 tumors)
- Recurrent liver cancer

Although the AJCC (TNM) staging system (see Liver Cancer Stages[1]) is often used to describe the spread of a liver cancer, doctors use a more practical system to determine treatment options. Liver cancers are often categorized as:

- Potentially resectable or transplantable cancer
- Unresectable (inoperable) cancer that has not spread
- Advanced cancer

Potentially resectable or transplantable liver cancer (stage I and some stage II cancers)

Potentially resectable

If your cancer is early stage and the rest of your liver is healthy, surgery (partial hepatectomy) may cure you. Only a small number of people with liver cancer are in this category. Important factors that may influence the outcome are the size of the tumor(s) and if nearby blood vessels are affected. Larger tumors or those that invade blood vessels are more likely to come back in the liver or spread elsewhere after surgery. How well your liver is working and your general health are also important. For some people with early-stage liver cancer, a liver transplant could be another option.

Clinical trials[2] are now looking at whether patients who have a partial hepatectomy will be helped by getting other treatments in addition to surgery. Some studies have found that using chemoembolization or other treatments along with surgery may help some patients live longer. More research is needed to know the value (if any) of adding other treatments to surgery.

Potentially transplantable

If your cancer is at an early stage, but the rest of your liver isn't healthy, you may be able to be treated with a liver transplant. A transplant may also be an option if the tumor is in a part of the liver that makes it hard to remove (such as very close to a large blood vessel). Candidates for liver transplant might have to wait a long time for a liver to become available. While they are waiting, they are often given other treatments, such as ablation or embolization, to keep the cancer under control.

Unresectable (inoperable) liver cancer that has not spread

Unresectable cancers include cancers that haven't yet spread to lymph nodes or distant parts of the body, but that can't be removed safely by partial hepatectomy. This might be because:

- The tumor is too large to be removed safely.

- The tumor is in a part of the liver that makes it hard to remove (such as very close to a large blood vessel).
- There are several tumors or the cancer has spread throughout the liver.
- The person isn't healthy enough for liver surgery.

Treatment options might include ablation, embolization, or both for the liver tumor(s). Other options may include targeted therapy, immunotherapy, chemotherapy (either systemic or by hepatic artery infusion), and/or radiation therapy

so they can treat them effectively.

Recurrent liver cancer

Cancer that comes back after treatment is called **recurrent**. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). Treatment of liver cancer that returns after initial therapy depends on many factors, including where it comes back, the type of initial treatment, and how well the

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