

Gemcitabine and cisplatin (GEM/CIS) for biliary tract cancers

If your doctor recommended the combination of gemcitabine and cisplatin to treat your cancer, here is some important information about these medications and some aspects related to them.

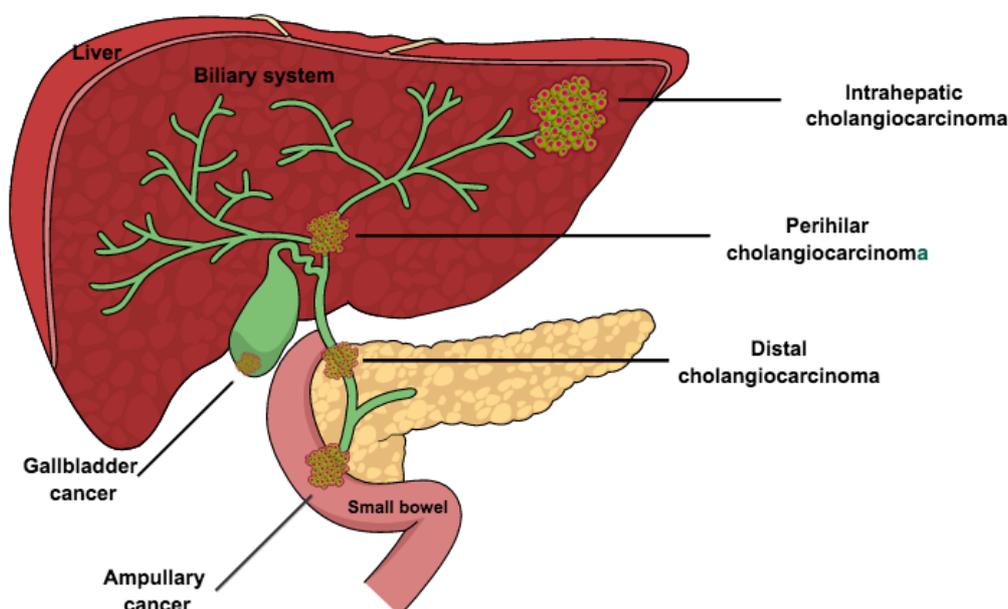
Biliary tract cancer

Cancers of the biliary tract develop from cells (called cholangiocytes) that normally make up the lining of the biliary system (depicted in green in the picture below). Biliary ducts are small tubes that carry the bile, which is used to digest food, from the liver and gallbladder into the small bowel.

Biliary tract cancers are cholangiocarcinoma, gallbladder cancer and ampullary cancer:

- **Cholangiocarcinoma** - which is also known as bile duct cancer. This cancer is categorised in three types, depending on where within the bile ducts it develops:
 - intrahepatic cholangiocarcinoma - when the cancer develops in the ducts inside the liver
 - perihilar cholangiocarcinoma - when it develops in the ducts just outside the liver
 - distal/extrahepatic cholangiocarcinoma - when it develops in the ducts further away from the liver
- **Gallbladder cancer** - arises from the gallbladder lining
- **Ampullary cancer** - arises from the join between the bile ducts and the small bowel

You have been given this leaflet because you have been diagnosed with a biliary tract cancer. Your oncologist can discuss with you which biliary tract cancer you have and how extended it is.



What is GEM/CIS?

Gemcitabine and cisplatin are two chemotherapy drugs which kill tumour cells by interfering with the process of cell replication. However, because they can also damage normal cells, they can cause some side effects. We will call the combination of gemcitabine and cisplatin with the shorter name GEM/CIS.

How are GEM/CIS administered?

You will receive GEM/CIS in hospital, in the chemotherapy unit. Both drugs are injected intravenously (into a vein) through a *cannula*, a short thin tube, which will be put into a vein in your arm or hand by a nurse. The cannula will be removed after you receive GEM/CIS. Because cisplatin may cause some pain or be harmful along the vein, you will receive plenty of fluids into your vein before and after the cisplatin infusion to prevent this.

Your doctor will decide the exact dosage of GEM/CIS you will receive based on many factors including your height, weight, age, general health and underlying conditions.

Schedule of GEM/CIS treatment

You will receive GEM/CIS in cycles of treatment. The standard schedule of GEM/CIS treatment follows a three-week cycle, involving one day of chemotherapy a week, for two weeks, followed by one week of rest.

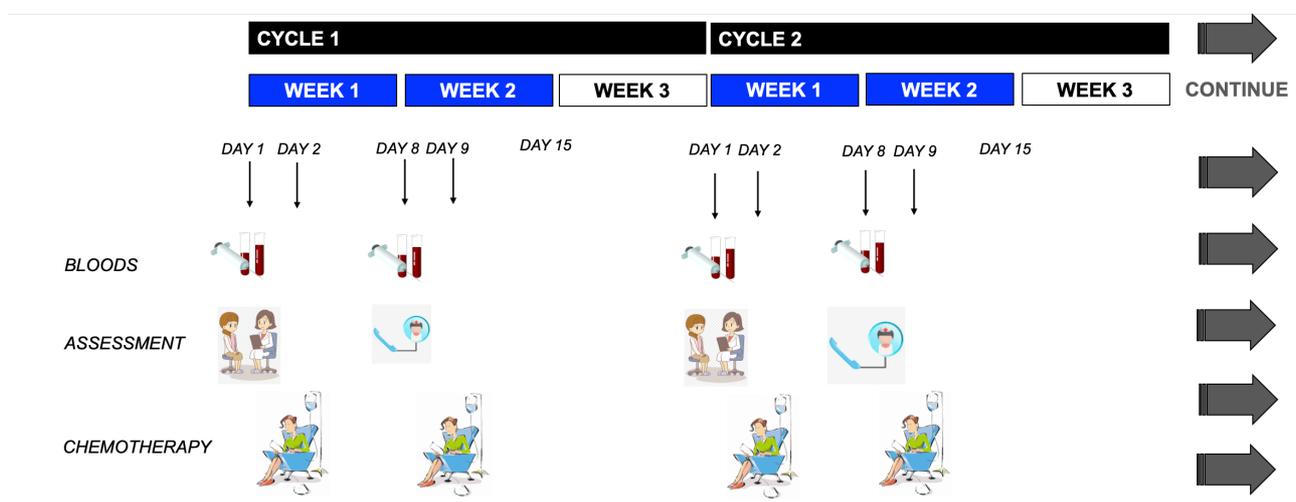
Before each session of chemotherapy, you will have a blood test and your oncological team will check whether you are fit enough for the chemotherapy session. It is important that you report any symptom(s) and problem(s) since your last session so that the dose/schedule can be adjusted and personalised specifically for you.

On DAY 1 of the first week of each cycle of chemotherapy, you will come to hospital to see the oncology team to be assessed and have a blood test. You will come back 1 or 2 days later to receive the chemotherapy. On this occasion you will not meet the doctor unless you have developed some issues. The chemotherapy session will last for 3 to 4 hours.

On DAY 8 of the second week you will need to repeat the bloods, but the team can assess you by phone before you come to hospital for your chemotherapy. The doctor may ask you to have the bloods taken at your GP practice the day before your chemotherapy appointment.

You will not need to stay in hospital overnight.

GEM/CIS cycle: 2 weeks on, 1 week off



Duration of GEM/CIS treatment

The doctor will discuss the duration of your treatment with you. Each GEM/CIS cycle will last for 3 weeks. If you are tolerating the treatment well, you will receive chemotherapy for at least 3 months before your doctor will advise a repeat scan to understand if the chemotherapy is working. If the first 3 months scan shows your cancer is stable or shrinking, your doctor may advise continuing the chemotherapy for another 3 months. After the first 6 months of treatment your doctor will discuss with you whether you should take a break from chemotherapy or if you should continue.

What are the side effects of the GEM/CIS treatment?

There are known side effects with this treatment, but you may not experience any of them. This does not mean that the treatment is not working; there is no relationship between the presence or severity of side effects and the efficacy of the medication.

You may get some of the side effects, but you are unlikely to get them all. Remember that side effects are often predictable in terms of their onset, duration and severity; they are almost always reversible and, except for those related to cisplatin, should completely go away after treatment. However, their frequency and severity vary from person to person.

As with many other chemotherapy drugs, GEM/CIS kill cancer cells because of their ability to stop cell division and proliferation. Unfortunately, chemotherapy drugs are not able to recognise the difference between the cancerous cells and normal cells. So, chemotherapy will also kill normal cells that are rapidly dividing, like blood cells, cells in the mouth, stomach, bowel and elsewhere, which is what causes some of the different side effects. Once treatment ends, those normal cells will grow back and be healthy.

There are many medications available that can be taken during chemotherapy to control and minimise the impact of any side effects you may have.

Some of the most common side effects related to GEM/CIS

Hematotoxicity: side effects on your blood cells including

- ***Low number of white blood cells and risk of infection***

Chemotherapy often reduces the number of white blood cells, which help you fight against infections. If your white blood cell count is too low (this is called *neutropenia*) you may be at risk of infections. At this time, it is important to be careful to avoid situations that could increase this risk of infections, such as being in crowded places or in touch with people with colds.

As the number of your white cells is most likely to be at its lowest between day 10 and day 14 of each of the cycles of your chemotherapy, during these days it is especially important to avoid risk of infection.

Reduction in white blood cells is one of the important blood checks your doctor will make before you receive your next dose of chemotherapy to ensure that the number of white blood cells is enough to protect you from infection while you receive chemotherapy.

It is important you are aware of the signs and symptoms of infection, and you must contact the helpline at your hospital if you develop any of the following:

- Your body temperature rises above 38°C (100.4°F), despite using paracetamol
- You suddenly feel shivery or unwell
- You develop a sore throat, a cough, diarrhoea, increased frequency of urination

- ***Low number of red blood cells***

Chemotherapy can reduce the number of red blood cells. The most important role of red blood cells is carrying oxygen to every part of your body. If the number of red blood cells is too low (this is called *anaemia*) you can feel tired and breathless. If your *anaemia* is severe, you will need a blood transfusion.

- ***Low number of platelets and risk of bruising or bleeding***

Chemotherapy can reduce the number of platelets. Platelets are useful to help the blood clotting. If your number of platelets is too low (this is called *thrombocytopenia*) you cannot receive chemotherapy and your doctor will delay your treatment for a short time until the platelet count improves. If you have any bruising or bleeding, such as nosebleeds, bleeding gums, tiny red or purple spots on the skin, please inform your doctor.

Flu-like symptoms: you may experience these during the chemotherapy treatment or shortly after:

- Feeling hot, cold or shivery
- Fever
- Headache
- Muscle pain
- Fatigue

Nausea: sometimes accompanied by vomiting but is usually well controlled by anti-sickness drugs (injections and tablets). You can experience it from a few hours to a few days after treatment. It is important to take anti-sickness medicines even if you don't feel sick, because it is easier to prevent sickness rather than treat it once it has started. Contact your doctor or nurse straight away if you've been feeling sick more than once in a day.

Fatigue: a very common side effect, which may increase during the treatment course.

Kidney damage (nephrotoxicity): this treatment can be harmful for kidneys, especially if you already have an underlying renal impairment. You will have blood tests before GEM/CIS treatment to check how well your kidneys are working. Your doctor will discuss with you and he/she will decide the best dose of chemotherapy for you in order to avoid further kidney damage. To help prevent damage, it is important to drink plenty of water. Your nurse might ask you to keep a record of how much you drink and of the amount of urine that you pass. Tell your doctor if you notice any changes in your urine, for example the presence of blood.

Hearing changes (ototoxicity): you might notice a ringing sound in your ears, called *tinnitus*. This often gets better on its own once the treatment ends. Rarely, it could be persistent for a long time after treatment ends. Let your doctor or nurse know if you notice any changes in your hearing.

Blood clotting: contact the helpline if your legs are swollen, red and sore or if you develop breathlessness.

Some less common side effects related to GEM/CIS

Allergic reaction: sometimes this happens while chemotherapy is given. Tell your doctor or nurse immediately if you have any of these sudden symptoms:

- rash
- shortness of breath
- redness or swelling of the face
- feeling hot
- dizziness
- need to pass urine

Numbness or tingling in fingers and toes (peripheral neuropathy): cisplatin-based chemotherapy can affect nerves by causing numbness, tingling or pain in the hands or feet. Numbness or tingling in fingers and toes can make it difficult to do fiddly things such as tying your shoelaces or doing up buttons. This might start within a few days or weeks and last for a few months. Rarely, the numbness may be permanent. You can find specific tips below to help to reduce these symptoms, if they occur.

Poor appetite: don't worry if you don't eat much for a day or two. Also your taste can change.

Diarrhoea: you need to get in touch with your team if you have 4 or more loose poos (stools) in 24 hours. Your doctor will give you anti-diarrhoea medicines. Remember to drink plenty of water to replace fluids lost. If you have diarrhoea you should eat low-fibre food and avoid raw fruits, fruit juice, cereals and vegetables. It can help to also avoid alcohol, caffeine, dairy products and high-fat foods.

Extravasation (leakage) of chemotherapy: While it is being administered, chemotherapy can sometimes leak outside the vein and damage the tissue around. Tell your nurse immediately if you have any stinging, pain, redness, or swelling around the vein.

Constipation: eating high-fibre foods (vegetables, fruit, wholemeal bread) and drinking at least 2 litres of water can help you. You may need laxatives if it lasts for longer than two/three days.

Mouth sores and ulcers: you need to brush your teeth every time after eating to avoid germs growing. Use a soft toothbrush and rinse three times a day with 1/2 to 1 teaspoon of baking soda mixed in water. It's better to avoid acidic foods such as oranges, lemons and grapefruits; tell your doctor or nurse if you have ulcers, as they can help to prevent or to treat mouth sores.

Drowsiness: chemotherapy may cause you to feel very sleepy (drowsy) and tired. If you feel very sleepy, do not drive or operate machinery.

Headache: if this happens, you may take painkillers like paracetamol.

Difficulty in sleeping: you can take sleeping tablets if you need them.

Hair loss: your hair may get thinner, but it is unlikely that you will lose your hair.

Skin changes: your skin may be drier or develop a rash.

Build-up of fluid: You may put on weight and your face or your ankles or legs may swell. It can help to put your legs up on a cushion. The swelling will get better after your treatment ends.

Medication to help control side effects

Make sure to let your doctor know of any side effects; there are useful medications to control the symptoms.

Should I continue to take all my usual medications?

Yes, you have to keep taking all your usual medications. Please report to your oncology team all the medications you are taking, so that they can advise.

Can I have the flu vaccination?

Yes, it is advised you have the flu vaccination before you start your chemotherapy. If you have already started your chemotherapy, please ask your doctor who can advise on the best timing to have the vaccination.

Tips during treatment

- Drink plenty of fluids (at least 2 litres per day) and protect your kidneys.
- Maintain good nutrition. Eating small frequent meals may help to reduce nausea. You should avoid fatty or fried foods. You can take anti-sickness drugs if you need.
- Avoid sun exposure. Wear SPF 15 (or higher) sunblock and protective clothing.
- Get plenty of rest.
- To prevent or minimize numbness and tingling:
 - avoid exposing your hands or feet to sudden changes of temperature. This can be helped by using gloves when you go for a walk in winter or by not touching frozen food/drink. Use oven gloves when cooking and protective gloves when gardening.
 - keep your hands and feet warm, wear well fitting, protective shoes.
 - Take care when using hot water as you may not be able to feel how hot it is and could burn yourself.
 - Take care when cutting your nails.
 - Moisturise your skin at least a couple of times a day.
- Keep at home the medications you may need to help control the symptoms.
- You may experience drowsiness or dizziness; avoid driving or engaging in tasks that require alertness until your response to chemotherapy is known.
- Use an electric razor when shaving and a soft toothbrush to minimize bleeding.
- Before starting chemotherapy, tell your doctor about any medication you are taking. Sometimes side effects may be related to your medicines and not to chemotherapy.

- If your symptoms are severe or do not improve after 24 hours, do not hesitate to contact the hospital.
- Pay attention to symptoms of a blood clot: pain, redness, swelling of an arm or a leg, breathlessness or chest pain. If you have any of these symptoms contact your doctor.
- Do not receive any kind of vaccination without your doctor's approval while taking chemotherapy.
- If you are a woman of childbearing age:
 - inform your doctor if you are pregnant or may be pregnant prior to starting this treatment.
 - avoid getting pregnant during chemotherapy.
 - do not breast feed during chemotherapy.

When to contact the hospital?

If your symptoms are severe or do not improve after 24 hours, do not hesitate to contact the hospital.

Hospital emergency contact:

Where can I get more information?

If you want to get more information in this field you can visit **ESMO** website for *Biliary tract cancer: Guide for Patients* and on the **AMMF** *The Cholangiocarcinoma Charity* website.

You can find the related link below:

<https://www.esmo.org/for-patients/patient-guides/biliary-tract-cancer>

<https://ammf.org.uk/cholangiocarcinoma/>