

What is
**Hepatocellular
Carcinoma?**

Let us answer some
of your questions.

Hepatocellular carcinoma

An ESMO guide for patients

Patient information based on ESMO Clinical Practice Guidelines

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand hepatocellular carcinoma and its treatment. It contains information on the causes of the disease and how it is diagnosed, up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

The medical information described in this document is based on the ESMO Clinical Practice Guideline for hepatocellular carcinoma, which is designed to help clinicians with the diagnosis and management of hepatocellular carcinoma. All ESMO Clinical Practice Guidelines are prepared and reviewed by leading experts using evidence gained from the latest clinical trials, research and expert opinion.

The information included in this guide is not intended as a replacement for your doctor's advice. Your doctor knows your full medical history and will help guide you regarding the best treatment for you.

Words highlighted in **colour** are defined in the glossary at the end of the document.

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Hepatocellular carcinoma: A summary of key information

The following information will be discussed in detail in this guide.

Introduction to hepatocellular carcinoma

- Liver cancer forms in the cells of the liver. The most common type of liver cancer is **hepatocellular carcinoma (HCC)**; this guide will focus exclusively on **HCC**.
- There are several known **risk factors** for **HCC**, including **liver cirrhosis**, long term infection with **hepatitis B virus (HBV)** or **hepatitis C virus (HCV)**, and other liver diseases such as **non-alcoholic fatty liver disease (NAFLD)** and **non-alcoholic steatohepatitis (NASH)**.
- Some of the **risk factors** for **HCC** can be reduced, for example by vaccination against **HBV** and early treatment of **HBV** and **HCV** infections.
- Patients with known **risk factors** for **HCC** can be monitored to ensure the disease is diagnosed at an early stage, giving the patient the best chance of successful treatment.
- Worldwide, liver cancer is the second most common cause of cancer death in men and the sixth most common cause of cancer death in women. **HCC** is more common in men and its incidence increases with age.

Diagnosis of hepatocellular carcinoma

- Early **HCC** often has no symptoms. Symptoms that may appear as the cancer progresses include weight loss, **jaundice** and pain/swelling in the abdomen.
- A diagnosis of **HCC** is usually based on the results of a **computed tomography (CT)** or **magnetic resonance imaging (MRI)** scan, which can show if there is a **tumour** in the liver.
- Further imaging and blood tests help to determine how advanced the cancer is. **HCC** is 'staged' according to the number/size of **tumours** and whether the cancer has spread to other parts of the body, as well as the patient's general health and liver function. This information is used to help decide the best treatment.

Treatment options for hepatocellular carcinoma

- Treatment for **HCC** depends on the size, location and stage of the **tumour**, and the general health of the patient.
- Patients should be fully informed and involved in decisions about treatment options.

Early-stage hepatocellular carcinoma

- Early-stage **HCC** is often treated with surgery to remove the **tumour (resection)**, as long as the remaining portion of liver is large enough to function well after surgery.
- Some patients with early-stage disease may be offered a liver transplant.
- Patients with very early-stage **HCC** can be suitable for treatment with **thermal tumour ablation** as an alternative to **resection**. This involves the use of heat to destroy **tumours** in the liver.

- **Radiotherapy** may sometimes be offered as an alternative option to surgery and **thermal tumour ablation**. The types of **radiotherapy** that may be used in this setting are **high dose rate (HDR) brachytherapy** (in which radioactive material is placed directly inside or next to the **tumour**), **stereotactic body radiotherapy (SBRT)**; in which **radiotherapy** is directed from a number of different positions around the body) and **selective internal radiotherapy (SIRT)**; in which radioactive microspheres are injected into the blood vessels supplying the liver).

Intermediate-stage hepatocellular carcinoma

- Intermediate-stage **HCC** is usually treated with **transarterial chemoembolisation (TACE)**. This involves injection of a **chemotherapy** drug directly into the blood vessel leading to the **tumour**, then blocking off the blood supply to starve the **tumour** of oxygen and nutrients.
- If **TACE** is unsuccessful or not possible, then **targeted therapy** (using drugs that block specific signalling pathways in cancer cells) may be offered. **SIRT** may be considered in patients unsuitable for **TACE** or **targeted therapy**.

Advanced-stage hepatocellular carcinoma

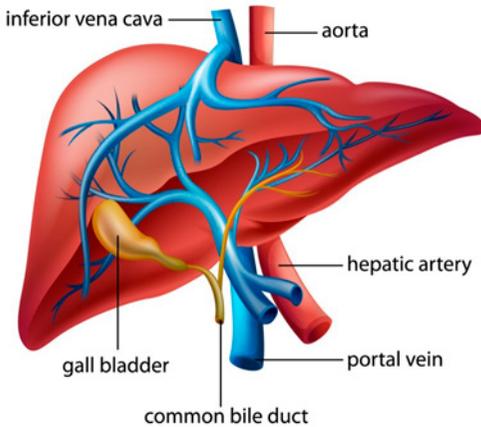
- Patients with advanced **HCC** who have satisfactory liver function and good general health are typically offered treatment with **targeted therapy**.
- **First-line** treatment options are **sorafenib** or **lenvatinib**. If the cancer continues to progress, then **regorafenib**, **cabozantinib** or **ramucirumab** may be offered to patients who received **sorafenib** previously.
- Patients with advanced **HCC** who have poor liver function and poor general health are usually offered supportive care, including pain relief and nutritional support.

Follow-up during/after treatment

- The timings of follow-up appointments vary between countries and practices. After **curative** treatment, follow-up appointments will usually include a clinical examination, blood tests and **CT** or **MRI** scans.
- Patients who experience a **recurrence** of their cancer can have further treatment. The treatment will depend on the extent of the **recurrence**, previous treatments received and the overall health of the patient.
- Support groups can help patients and their families to better understand **HCC** and to learn how to cope with all aspects of the disease, from diagnosis to long-term effects.
- The European Liver Patients' Association (ELPA) brings together patient groups to promote the interests of people with liver disease: <https://elpa.eu>.

What is the liver?

The liver is a large organ located below the right lung, which has a number of important functions. It stores nutrients from food and converts them into energy when required. It also produces **bile**, which is a fluid that helps to digest food, and breaks down harmful substances so that the body can excrete them in urine or faeces.



*Anatomy of the liver showing the position of major blood vessels, **bile ducts** and the **gallbladder**.*

What is liver cancer?

Liver cancer is a cancer that forms in the cells of the liver. The liver consists of different types of cells, and liver cancer is classified by the type of cell it starts in.

The most common form of liver cancer is **hepatocellular carcinoma (HCC)**, which starts in the main liver cells (**hepatocytes**). This guide will focus exclusively on **HCC**.

HCC is the most common type of liver cancer

Other rarer types of liver cancer include:

- **Fibrolamellar carcinoma:** A rare type of **HCC** that usually develops in young people.
- **Cholangiocarcinoma:** Cancer that starts in the **bile ducts** in the liver.
- **Angiosarcoma:** Cancer that develops in the blood vessels within the liver.
- **Hepatoblastoma:** A very rare liver cancer that usually affects young children.

What are the symptoms of hepatocellular carcinoma?

There are often no symptoms of **HCC**, particularly in the early stages. However, if there are symptoms, they may include:

- Weight loss.
- Yellowing of the skin and whites of the eyes (**jaundice**).
- Itching.
- Feeling sick.
- Swollen abdomen.
- Loss of appetite.
- Pain in the abdomen or right shoulder.
- Lump on the right side of the abdomen.

You should see your doctor if you experience any of these symptoms. However, it is important to remember that these symptoms can also occur in people who do not have **HCC**; they may also be caused by other conditions.



HCC often has no symptoms in the early stages

How common is liver cancer?

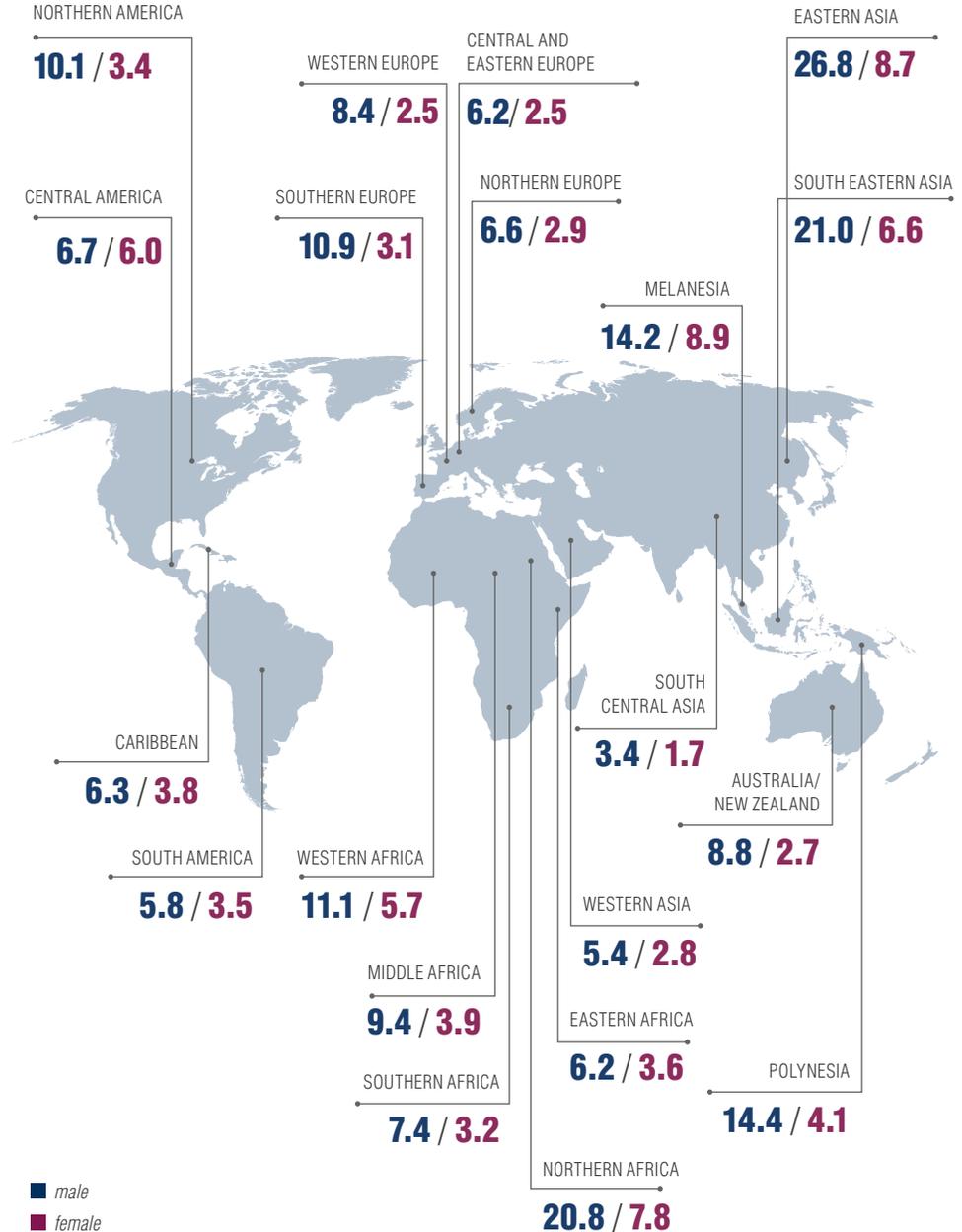
Liver cancer is the second most common cause of cancer death in men and the sixth most common cause of cancer death in women (*Ferlay et al., 2018*). **HCC** is more common in men and its incidence increases with advancing age (*Vogel et al., 2018*).

HCC is more common in men than in women

The highest incidences of liver cancer have been reported in Eastern Asia. The lowest incidences are in South Central Asia (*Ferlay et al., 2018*). Regional differences in incidence rates reflect the geographical distribution of **hepatitis B virus (HBV)** and **hepatitis C virus (HCV)**, which are the most prominent causes of **HCC** (see section '*What causes hepatocellular carcinoma?*' for more information).

Hepatocellular Carcinoma

The map shows estimated numbers of new cases of liver cancer diagnosed in 2018 per 100,000 people of each region's population (Ferlay et al., 2018).



What causes hepatocellular carcinoma?

Several **risk factors** for developing **HCC** have been identified. It is important to remember that having a **risk factor** increases the risk of cancer developing but it does not mean that you will definitely get cancer. Likewise, not having a **risk factor** does not mean that you definitely won't get cancer.

Several risk factors have been identified for HCC



FACTORS THAT MAY INCREASE RISK

Liver cirrhosis

HBV

HCV

Non-alcoholic fatty liver disease (NAFLD)

Non-alcoholic steatohepatitis (NASH)

Excessive alcohol intake

Diabetes

Being overweight

Smoking

Increasing age

HIV or AIDS

Aflatoxin intake

Family history of liver cancer

*There are various **risk factors** associated with developing **HCC** although each factor may not apply to everyone who develops the disease.*

Long-term infection with **HBV** or **HCV** is a major **risk factor** for the development of **HCC**. Incidence rates for **HCC** are highest in regions with high rates of **HBV** and **HCV**, such as Africa and Asia. Lifestyle also has a substantial impact on the risk of developing **HCC**. For example, rates of obesity and type 2 **diabetes** have increased in recent decades, leading to a rise in **NAFLD** and **NASH**. **NAFLD** and **NASH** are both liver diseases that can lead to **liver cirrhosis** and **HCC** (Vogel et al., 2018).

Prevention and screening

The link between liver disease and **HCC** means that steps can be taken to prevent development of **HCC**. For example, vaccination against **HBV** at birth can eliminate **HBV** as a **risk factor**. Early treatment of patients with **HBV** or **HCV** can also prevent development of **HCC** (Vogel et al., 2018).

There is no routine screening programme for **HCC**; however, patients with certain conditions that place them at a higher risk of developing the disease may be closely monitored. For example, patients with **liver cirrhosis** typically undergo **ultrasound** scans every 6 months to check for the development of **HCC** (Vogel et al., 2018). Patients with long-term **HBV** or **HCV** infection may also be monitored in this way. This ensures that **HCC** is diagnosed at an early stage, and gives the patient the best chance of successful treatment.

Patients with certain risk factors may be monitored for the development of HCC

How is hepatocellular carcinoma diagnosed?

A diagnosis of **HCC** is based on the results of the following examinations and tests:

Clinical examination

If you have symptoms of **HCC**, your doctor may carry out a general clinical examination to feel any areas of your abdomen that are swollen or painful.

Blood tests

Your doctor may recommend that you have a blood test to check how well your liver is functioning, and to look for the presence of any **risk factors** for **HCC**, such as **HBV** or **HCV**.

You may also have a test to check the levels of a **tumour biomarker** called **alpha fetoprotein (AFP)**. People with **HCC** might have raised levels of **AFP** in their blood. However, it is important to understand that some people with **HCC** don't have raised levels of **AFP**, and that raised **AFP** levels can also occur in other conditions, including **liver cirrhosis**. For these reasons, a blood test alone cannot provide a diagnosis.



Clinical examination and a blood test can indicate if further tests are needed

Imaging

Your doctor may recommend that you have a **computed tomography (CT)** or **magnetic resonance imaging (MRI)** scan to look at your liver for signs of cancer (Vogel et al., 2018). **CT** is a type of **x-ray** technique that lets doctors see your internal organs in cross-section. **MRI** uses magnetic fields and radio waves to produce detailed images of the inside of the body. **CT** and **MRI** are often used in the diagnosis of **HCC**, as they allow doctors to examine the blood vessels around a suspicious mass, which helps to ascertain whether the mass is cancerous or not (Vogel et al., 2018).

Some patients may be offered an **ultrasound** scan to help with diagnosis of **HCC** (Vogel et al., 2018). A handheld **ultrasound** scanner is placed onto the abdomen and produces sound waves to create a picture of the internal organs.

HCC is usually diagnosed using imaging tests

Biopsy

Your doctor may wish to take a **biopsy** from your liver. This involves taking samples of tissue from the liver to look for cancer cells. However, a **biopsy** is usually not needed as doctors can often diagnose **HCC** from imaging tests alone.

If you do have a **biopsy**, it may be taken through the skin of your abdomen (called a **percutaneous biopsy**) or by keyhole surgery (**laparoscopy**). Your doctor will explain the options available to you.



How will my treatment be determined?

Your treatment will largely depend on the stage of your cancer.

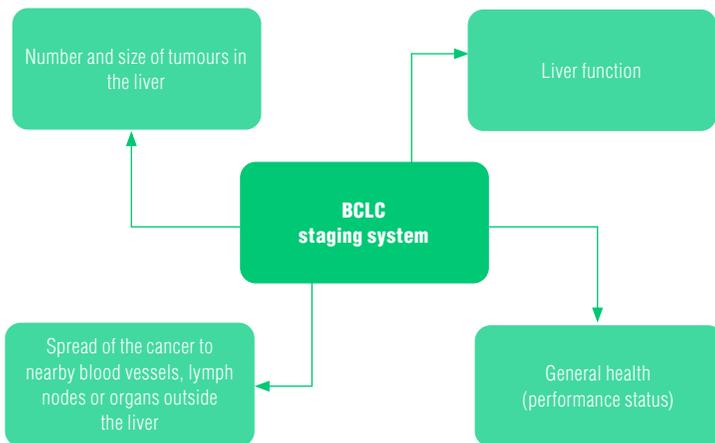
Staging

Staging is used to describe the extent of the cancer overall; this includes its size and position and whether it has spread from where it started. For **HCC**, staging is usually based on **MRI** or **CT** scans of the abdomen, pelvis and chest in combination with blood tests to evaluate liver function and **AFP** levels (Vogel *et al.*, 2018).

Imaging scans can show if the cancer has spread to other parts of the body



In Europe, staging to determine the size and spread of **HCC** is usually described using the **Barcelona Clinic Liver Cancer (BCLC)** system. There are five **BCLC** stages designated 0, A, B, C and D. Generally, the lower the stage, the better the outcome (or **prognosis**) for the patient. The **BCLC** staging system considers the factors shown in the figure below.



Considerations included in the **BCLC** staging system.

Staging helps to determine the most appropriate treatment for HCC

General health (known as **performance status**) is graded 0–5, where 0 is fully active, 4 is completely disabled and 5 is deceased.

The staging criteria for **HCC** is described in the table below (Vogel et al., 2018; Llovet et al., 2008). This may seem complicated but your doctor will be able to explain which parts of this table correspond to your cancer, and how the stage of your cancer impacts on treatment choice.

BCLC stage 0	<ul style="list-style-type: none">• Single tumour <2 cm• Good liver function• Performance status 0
BCLC stage A	<ul style="list-style-type: none">• Single tumour of any size or up to 3 tumours <3 cm• Satisfactory liver function• Performance status 0
BCLC stage B	<ul style="list-style-type: none">• Multiple tumours• Satisfactory liver function• Performance status 0
BCLC stage C	<ul style="list-style-type: none">• Cancer has spread into the portal vein• Cancer has spread to lymph nodes or organs outside the liver• Satisfactory liver function• Performance status 1–2
BCLC stage D	<ul style="list-style-type: none">• End-stage liver function• Performance status 3–4

BCLC stage grouping system for **HCC**. Adapted from Llovet et al., 2008.

What are the treatment options for hepatocellular carcinoma?

Your treatment will depend upon the size, location and stage of the **tumour**, as well as your general health and level of fitness. The choice of treatments will be discussed with you and your preferences will be taken into account. Your treatment will be discussed by a **multidisciplinary team**, which means that experts in different areas of cancer treatment (e.g. oncologists, surgeons, gastroenterologists, radiologists and nurses) come together to share their expertise in order to provide the best patient care.



It is important that patients are fully involved in the treatment decision-making – when there are several treatments available, doctors should involve patients in making decisions about their care so that they can choose the care that meets their needs and reflects what is important to them. This is called ‘shared decision-making’.

It is important that patients are fully involved in discussions and decisions about their treatment

Your doctor will be happy to answer any questions you have about your treatment. Four simple questions that may be helpful when talking with your doctor or any healthcare professional involved in your care are shown below.

“What treatment options do I have?”

“What are the possible advantages and disadvantages of these treatment options?”

“How likely am I to experience benefits or side effects?”

“Are there any clinical trial options?”

Your doctor may recommend one or more of the following approaches for treating **HCC**:

Surgery

Surgery gives the best chance of curing **HCC**. Two types of surgery can be used in the treatment of **HCC**: **resection** and liver transplant.

Resection

The aim of **resection** is to remove the cancer along with a healthy **margin** of tissue to help stop it from coming back. **Resection** is usually only offered to patients with early-stage disease (**BCLC** stage 0–A), when there is a good chance of complete **resection**. Liver function tests are carried out before **resection** to check that the remaining liver tissue will work well enough after the operation. Patients with **liver cirrhosis** may not have enough healthy liver to cope with **resection**, so this type of surgery may not be suitable for these patients.



Surgical removal of the tumour offers the best chance of cure for HCC

Transplant

Liver transplant can cure both the **HCC** and any underlying liver disease. However, transplant is usually only offered to patients with early-stage disease when there is a good chance of cure, and patients may have to wait a long time for a suitable liver to become available for transplant. As the **HCC** may grow during this waiting time, patients might be offered other types of treatment to minimise the risk of **tumour** progression.

Thermal tumour ablation

Thermal tumour ablation uses heat to destroy **tumours** in the liver. Probes are inserted through the skin to deliver the heat to the **tumour**. The heat only travels a short distance, so it doesn't affect the rest of the liver. There are two types of **thermal tumour ablation**: **radiofrequency ablation** uses a high-frequency electric current to heat the cancer cells, while **microwave ablation** uses microwaves to create the heat. **Thermal tumour ablation** works best on small **tumours** and may be recommended for patients who are not suitable for **resection**.

Transarterial chemoembolisation

Transarterial chemoembolisation (TACE) involves injection of a **chemotherapy** drug (usually **doxorubicin** or **cisplatin**) directly into the blood vessel that is feeding the **tumour**, then blocking off the blood supply to starve the **tumour** of oxygen and nutrients. A **catheter** is inserted into a blood vessel in the groin and is fed into the body until it reaches the liver. A dye is then injected and **x-rays** are used to see the blood vessels that are feeding the **tumour**. **Chemotherapy** is injected into the appropriate blood vessels and then particles are injected to block the blood supply – this is known as conventional lipiodol-based **TACE**. An alternative type of **TACE**, called **doxorubicin-eluting bead TACE**, involves the injection of beads into the blood vessels, which block the blood supply and slowly release **chemotherapy**.

TACE may be offered to patients with early- or intermediate-stage disease who are not suitable for surgery, or to patients who are waiting for a liver transplant.

TACE blocks the blood supply to a tumour after chemotherapy is administered

Radiotherapy

Radiotherapy uses **ionising radiation** to damage the **DNA** of cancerous cells, causing them to die. Various types of **radiotherapy** can be used in the treatment of **HCC**, including:

- **High dose rate (HDR) brachytherapy**: radioactive material is placed directly inside or next to the **tumour**.
- **Stereotactic body radiotherapy (SBRT)**: **radiotherapy** is directed from a number of different positions around the body, with the radiation beams meeting at the **tumour**.
- **Selective internal radiotherapy (SIRT)**: radioactive microspheres are injected into the blood vessels supplying the liver.

Targeted therapy

Targeted therapies are drugs that block specific signalling pathways in cancer cells that encourage them to grow. A number of **targeted therapies** are now available for the treatment of **HCC**. These treatments are usually offered to patients with advanced disease, who are not suitable for other types of therapy. **Targeted therapies** used in **HCC** include **sorafenib**, **lenvatinib**, **regorafenib**, **cabozantinib** and **ramucirumab**. **Sorafenib**, **lenvatinib**, **regorafenib** and **cabozantinib** are taken daily by mouth, whereas **ramucirumab** is administered into a vein every 2 weeks.

A number of targeted therapies are now available for the treatment of HCC

Immunotherapy

Immunotherapies are treatments that block inhibitory pathways which restrict the body's immune response to cancer, thereby helping to reactivate the body's immune system to detect and fight the cancer.

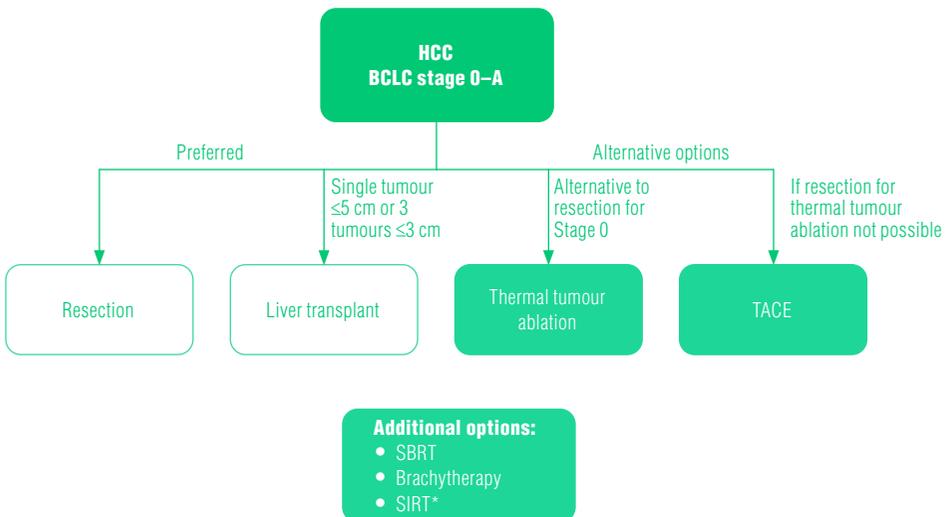
Immunotherapies are not yet approved for the treatment of **HCC** in Europe, but several have been evaluated in **clinical trials**, including **atezolizumab** (in combination with the **targeted therapy bevacizumab**), **nivolumab** and **pembrolizumab**.

What are the treatment options for early-stage hepatocellular carcinoma (BCLC stage 0–A)?

Early-stage **HCC** is often treated with **resection**, as long as the remaining liver is judged to be large and functional enough to cope after surgery. This is usually done via **laparoscopy** (keyhole surgery).

Patients with one **tumour** that is no larger than 5 cm or three **tumours** that are each no larger than 3 cm may be suitable for a liver transplant. If waiting for a transplant for more than 3 months, patients might be offered other treatments such as **resection**, **thermal tumour ablation**, **TACE** or **SIRT** to minimise the risk of **tumour** progression before transplant (Vogel *et al.*, 2018).

Patients with very early-stage **HCC** (**BCLC** stage 0) might be considered for **thermal tumour ablation** as an alternative to **resection**, as it is associated with similar outcomes and is less invasive. **TACE** is not usually a **first-line** option for patients with early-stage **HCC** but may be considered for patients who are not suitable for **resection** or **thermal tumour ablation**. In some patients, **HDR brachytherapy**, **SBRT** or **SIRT** might be considered as alternative options (Vogel *et al.*, eUpdate 2020).



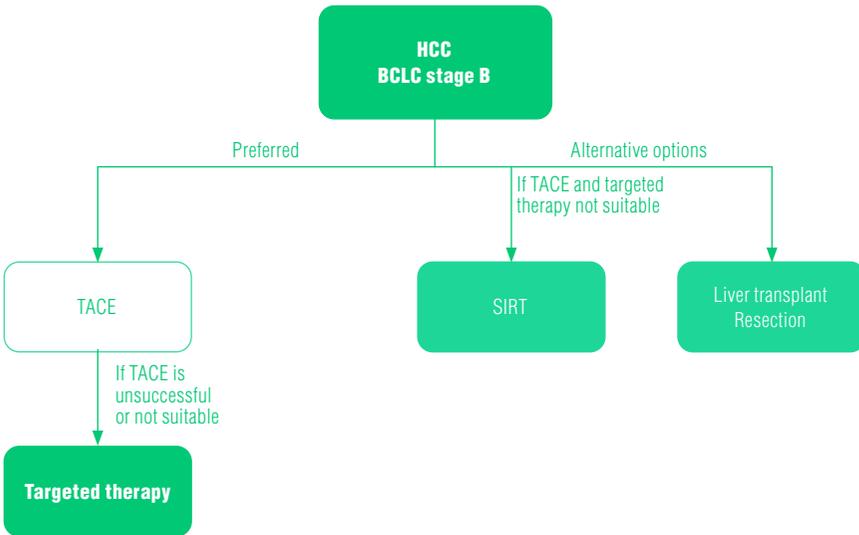
*May be considered in exceptional circumstances when neither **TACE** nor systemic therapy is possible

Treatment options for early-stage **HCC**.

What are the treatment options for intermediate-stage hepatocellular carcinoma (BCLC stage B)?

TACE is the standard **first-line** treatment for intermediate-stage **HCC**, as long as the **tumour** is accessible for the procedure. If **TACE** is unsuccessful or not possible, then **targeted therapy** may be considered. In a minority of patients who are unable to have **TACE** or **targeted therapy**, **SIRT** is a possible alternative option (Vogel et al., eUpdate 2020).

Resection or liver transplant may be considered for some patients, but this is less common than in early-stage **HCC**.



Treatment options for intermediate-stage **HCC**.

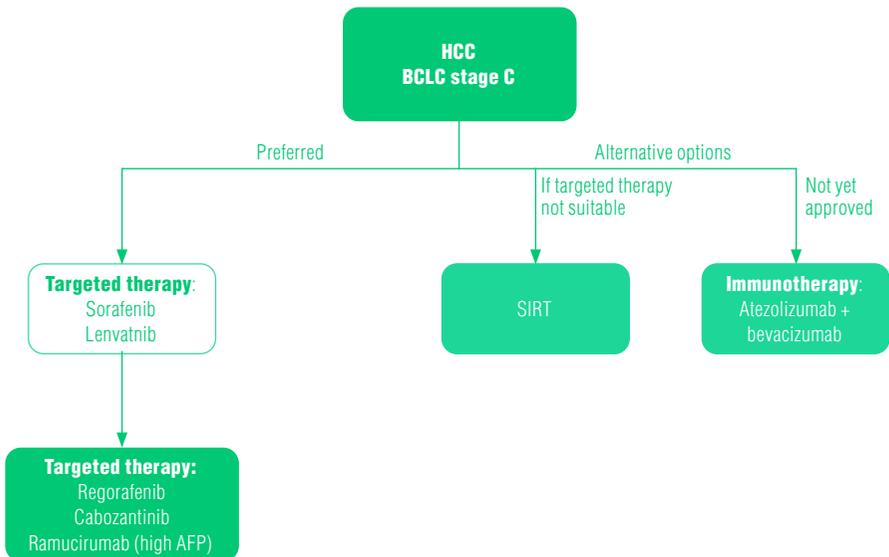
What are the treatment options for advanced-stage hepatocellular carcinoma (BCLC stages C and D)?

Patients with advanced **HCC** who have satisfactory liver function and good general health (**BCLC** stage C) are usually treated with **targeted therapy**.

First-line treatment is typically **sorafenib** or **lenvatinib**. If the cancer progresses on **sorafenib**, a number of **second-line targeted therapy** options are available. These include **regorafenib**, **cabozantinib** and **ramucirumab** (in patients with high **AFP** levels) (*Vogel et al., eUpdate 2020*).

In patients with advanced **HCC** who are not suitable for treatment with **targeted therapies** but who have good liver function, **SIRT** might be considered.

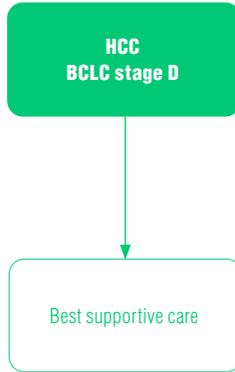
Immunotherapy with **atezolizumab** in combination with the **targeted therapy bevacizumab** may be considered in patients with advanced **HCC**, based on the results of a recent **clinical trial** that showed **first-line** treatment with **atezolizumab + bevacizumab** led to better outcomes than **sorafenib** (*Cheng et al., 2019*). However, it is important to understand that this treatment is currently not approved for the treatment of **HCC** in Europe. More data are needed to fully understand the possible benefits of **atezolizumab + bevacizumab** in **HCC**.



Treatment options for **BCLC** stage C **HCC**.

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Patients with advanced **HCC** who have poor liver function and poor general health (**BCLC** stage D) are unlikely to cope with any of the treatments summarised above. These patients are usually offered supportive care (see section '*Additional interventions*' for more information), including pain management, nutrition and psychological support.



*Treatment for **BCLC** stage D **HCC**.*

Clinical trials

Your doctor may ask whether you would like to take part in a **clinical trial**. This is a research study conducted with patients in order to (*ClinicalTrials.gov, 2019*):

- Test new treatments.
- Look at new combinations of existing treatments or change the way they are given to make them more effective or reduce side effects.
- Compare the effectiveness of drugs used to control symptoms.

Clinical trials help to improve knowledge about cancer and develop new treatments, and there can be many benefits to taking part. You will have to undergo various tests before entering a trial and be carefully monitored during and after the study. Although the new treatment

may offer benefits over existing therapies, it's important to bear in mind that some new treatments are found not to be as good as existing treatments or to have side effects that outweigh the benefits (*ClinicalTrials.gov, 2019*).



Clinical trials help to improve knowledge about diseases and develop new treatments – there can be many benefits to taking part

There are a number of **clinical trials** ongoing to evaluate new treatments for **HCC**. A recent study reported improved survival with **first-line atezolizumab + bevacizumab** compared with **sorafenib** (*Cheng et al., 2019*), and as a result, this treatment might be an option for some patients with advanced **HCC** (see section 'What are the treatment options for advanced-stage hepatocellular carcinoma (BCLC stages C)?' for more information). An **immunotherapy** called **nivolumab** has been studied as a **first-line** treatment for patients with **HCC**, but the trial showed that there was no significant difference in survival compared with **sorafenib** (*Yau et al., 2019*). Another **immunotherapy**, **pembrolizumab**, underwent evaluation in patients with **HCC** who had previously been treated with **sorafenib**; however, **pembrolizumab** showed no significant improvement in survival compared with best supportive care (*Finn et al., 2019*).

It is important to understand that **immunotherapy** is a rapidly evolving field of research. Scientists and doctors are working to establish the potential use of **immunotherapy** in **HCC** and to identify which patients are most likely to benefit. **Immunotherapies** are not currently approved for the treatment of **HCC** in Europe.

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You have the right to accept or refuse participation in a **clinical trial** without any consequences for the quality of your treatment. If your doctor does not ask you about taking part in a **clinical trial** and you want to find out more about this option, you can ask your doctor if there is a trial for your type of cancer taking place nearby (*ClinicalTrials.gov, 2019*).

The European Medical Association has a register of all European clinical trials. You can find it here: www.clinicaltrialsregister.eu/

Additional interventions

Patients may find that supplementary care helps them to cope with their diagnosis, treatment and the long-term effects of treatment for HCC

During the course of your disease, anti-cancer treatments should be supplemented with interventions that aim to prevent the complications of disease and treatment, and to maximise your quality of life. These interventions may include supportive, **palliative**, survivorship and end-of-life care, which should all be coordinated by a **multidisciplinary team** (Jordan et al., 2018). Ask your doctor or nurse about which additional interventions are available; you and your family may receive support from several sources, such as a **dietician**, social worker, priest or other spiritual advisor, physiotherapist or occupational therapist.

Supportive care

Supportive care involves the management of cancer symptoms and the side effects of therapy. Many patients with **HCC** suffer from malnutrition and experience weight loss and muscle wasting. A **dietician** will be able to advise you on your diet and any supplements that you might need. You may be offered nutritional supplements to increase your calorie intake – this can help you to stay healthier during treatment.

Palliative care

Palliative care is a term used to describe care interventions in advanced disease, including the management of symptoms as well as support for coping with **prognosis**, making difficult decisions and preparation for end-of-life care. **Palliative** care in patients with **HCC** may include treatment for pain, fluid retention, nausea, nutritional problems and constipation (Kumar and Panda, 2014).

Survivorship care

Support for patients surviving cancer includes social support, education about the disease and rehabilitation. For example, psychological support can help you to cope with any worries or fears.

Psychosocial problems impacting on your quality of life may include concerns about the cancer returning and the long-term effects of your treatment. Patients often find that social support is essential for coping with the cancer diagnosis, treatment and the emotional consequences. A survivor care plan can help you to recover wellbeing in your personal, professional and social life. For further information and advice on survivorship, see ESMO's patient guide on survivorship (www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship).



End-of-life care

End-of-life care for patients with incurable cancer primarily focusses on making the patient comfortable and providing adequate relief of physical and psychological symptoms, for example **palliative** sedation to induce unconsciousness can relieve severe pain, breathlessness (**dyspnoea**), or delirium (*Cherny, 2014*). Discussions about end-of-life care can be upsetting, but support should always be available to you and your family at this time. Your doctor or nurse will help to guide you through the options available.

What are the possible side effects of treatment?

As with any medical treatment, you may experience side effects from your anti-cancer treatment. The most common side effects for each type of treatment are highlighted below, along with some information on how they can be managed. You may experience side effects other than those discussed here. It is important to talk to your doctor about any potential side effects that are worrying you.

Doctors classify side effects from any cancer therapy by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, grade 1 side effects are considered to be mild, grade 2 moderate, grade 3 severe and grade 4 very severe. However, the precise criteria used to assign a grade to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your doctor as soon as possible.



It is important to talk to your doctor about any treatment-related side effects that are worrying you

Fatigue is very common in patients undergoing cancer treatment and can result from either the cancer itself or the treatments. Your doctor can provide you with strategies to limit the impact of **fatigue**, including getting enough sleep, eating healthily and staying active (*Cancer.Net, 2018*). Loss of appetite and weight loss can also arise due to the cancer itself or the treatments. Significant weight loss, involving loss of both fat and muscle tissue, can lead to weakness, reduced mobility and loss of independence, as well as anxiety and depression (*Escamilla and Jarrett, 2016*). Your doctor may refer you to a **dietician** who can look at your nutritional needs and advise you on your diet and any supplements that you might need.

Surgery

Resection for HCC is a major operation and it will take some time to recover – you may have to stay in hospital for at least a few days. It is normal to experience pain for the first week or so and your doctor or nurse will be able to give you painkillers to help keep you feeling comfortable. You will be encouraged to move around as soon as possible after your operation to speed up your recovery; however, it is normal to feel tired for several weeks after surgery. There is an increased risk of bleeding after liver surgery, so you will be closely monitored during and

Hepatocellular Carcinoma

after the operation, and may be given a **blood transfusion** if bleeding occurs. There is also a risk of **bile** leakage from the liver after surgery, which can cause pain and sickness. Another operation may be needed to repair the **bile** leak, although this is uncommon.

Following a liver transplant, it is common to have some bleeding for a couple of days after the operation, while the new liver begins to function. A **blood transfusion** might be needed if you lose a lot of blood. Your kidneys may stop working properly after the transplant – they usually recover, but some patients need to have **dialysis** for a few weeks until their kidneys start working again. As with **resection**, there is a risk of **bile** leakage after transplant.

There is also a possibility that your body will reject the new liver; to prevent this, you will be given anti-rejection medicines to stop your immune system from attacking the new liver. The anti-rejection medicines can increase the risk of serious infections, especially in the first few months after the transplant. You can minimise your risk of infection by staying away from anyone who has an infection, and by avoiding eating raw fish/eggs, mould-ripened cheeses and unpasteurised yoghurts and milk. The anti-rejection medications may also cause kidney damage, **hypertension**, high cholesterol, **diabetes** and bone thinning, which you will be monitored for. It is especially important to eat a well-balanced diet that is low in salt, cholesterol, fat and sugar after a liver transplant to reduce the risk of these side effects and keep your new liver healthy.

A liver transplant is a major operation and may have long-term health implications

Thermal tumour ablation

Following **thermal tumour ablation**, you will normally have to stay in bed for a few hours, but you should be able to go home the next day. You might have some discomfort or mild pain, which can be treated with painkillers. Some people have flu-like symptoms for up to a week after treatment. This is normal, but you should contact your doctor or nurse if you feel unwell after this time or have a fever, as you may have an infection. There is a very small risk of damage to the liver, **bile ducts** or other organs near the liver during **thermal tumour ablation**, but this is very rare.

Transarterial chemoembolisation

After treatment with **TACE**, you will need to stay lying down for 4 to 6 hours afterwards and will probably stay in hospital for 1 or 2 nights. Common side effects of **TACE** include nausea, vomiting, abdominal pain and fever – these are normal and can last for a few days. **Fatigue** is also common and may last for a few weeks. Rarer side effects include damage to blood vessels, leakage of dye out of blood vessels and allergic reaction to the dye. There is also a risk that some of the **chemotherapy** drug can flow out of the liver and enter the bloodstream, causing side effects such as an increased risk of infection, **fatigue**, breathlessness, a sore mouth and hair loss – these effects are temporary.

Radiotherapy

Common side effects of **SBRT** and **HDR brachytherapy** include **fatigue**, nausea, vomiting and diarrhoea. **SBRT** may also cause redness of the skin (like mild sunburn) in the treatment area. **Fatigue** from **radiotherapy** usually starts during treatment and lasts for about a week after you have finished treatment. Nausea and vomiting are usually mild, but you can ask your doctor or nurse for anti-sickness tablets to help with this. If the nausea affects your appetite, your doctor or nurse might suggest a high-calorie supplement to ensure you are getting enough nutrition. Diarrhoea as a side effect of **radiotherapy** is usually mild and you may not experience it at all. If you do have diarrhoea, you should drink plenty of fluids to avoid becoming dehydrated. A low-fibre diet can help, and if necessary, your doctor or nurse might give you medications to help slow down your bowel.

SIRT is associated with a number of mild side effects including fever, chills, nausea, diarrhoea, stomach ache and a feeling of pressure in the abdomen. Rarely, some of the radioactive microspheres can travel to the **gastrointestinal system**, which can cause pain in the abdomen, vomiting, bleeding and stomach ulcers. To prevent irritation, you may be given anti-ulcer medication.

Targeted therapies

Common side effects in patients treated with **targeted therapies** include effects on the **gastrointestinal system** (e.g. diarrhoea, nausea), skin problems (e.g. **hand-foot syndrome**) and **hypertension** (high blood pressure).

Many of the side effects from **targeted therapies** can be prevented or managed effectively. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking a **targeted therapy**.

The table below lists the most important specific side effects of **targeted therapy** drugs used in the treatment of **HCC**.



Hand-foot syndrome - redness, swelling, pain and blisters can occur on the palms of the hands and/or the soles of the feet.

TARGETED THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
<p>Cabozantinib (<i>Cabometyx SPC, 2019</i>)</p>	<ul style="list-style-type: none"> • Decreased appetite • Diarrhoea • Fatigue • Hand-foot syndrome • Hypertension • Nausea 	<ul style="list-style-type: none"> • Effects on the gastrointestinal system (e.g. nausea, diarrhoea) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects • To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment • Your blood pressure will be monitored during treatment and anti-hypertensive treatment will be given if necessary
<p>Lenvatinib (<i>Lenvima SPC, 2019</i>)</p>	<ul style="list-style-type: none"> • Decreased appetite • Decreased weight • Diarrhoea • Fatigue • Hypertension 	<ul style="list-style-type: none"> • Effects on the gastrointestinal system (e.g. diarrhoea) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects • Your blood pressure will be monitored during treatment and anti-hypertensive treatment will be given if necessary
<p>Ramucirumab (<i>Cyramza SPC, 2019</i>)</p>	<ul style="list-style-type: none"> • Diarrhoea • Fatigue • Leukopenia • Neutropenia • Nose bleeds • Stomatitis 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored by frequent blood tests throughout your treatment in order to detect leukopenia or neutropenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections • Your doctor or nurse will be able to help you to prevent or manage effects on the gastrointestinal system (e.g. diarrhoea) • To prevent and treat stomatitis, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (grade 2 and above) stomatitis, your doctor may suggest lowering the dose of treatment, or delaying therapy until the stomatitis resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment • Let your doctor know if you experience nose bleeds so that they can decide how to manage these

TARGETED THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Regorafenib <i>(Stivarga SPC, 2019)</i>	<ul style="list-style-type: none"> Decreased appetite Diarrhoea Fatigue Hand-foot syndrome Hypertension Infection Pain 	<ul style="list-style-type: none"> Effects on the gastrointestinal system (e.g. diarrhoea) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment Your blood pressure will be monitored during treatment and anti-hypertensive treatment will be given if necessary Let your doctor know if you experience pain or any symptoms of infection (e.g. fever, chills, cough) so that they can decide how to manage these
Sorafenib <i>(Nexavar SPC, 2019)</i>	<ul style="list-style-type: none"> Alopecia Diarrhoea Fatigue Hand-foot syndrome Infection Rash 	<ul style="list-style-type: none"> Your doctor or nurse will be able to help you to prevent or manage effects on the gastrointestinal system (e.g. diarrhoea) To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment Alopecia can be upsetting for many patients; your doctor can provide you with information on how to cope with this side effect Let your doctor know if you experience a rash or any symptoms of infection (e.g. fever, chills, cough) so that they can decide how to manage these

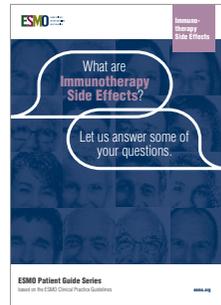
Important side effects associated with individual targeted therapy drugs used in the treatment of HCC.

The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at www.ema.europa.eu/ema/.

Immunotherapy

Common side effects in patients treated with **immunotherapy** include effects on the skin (e.g. rash, **pruritus**) and **gastrointestinal system** (e.g. diarrhoea, nausea). Many of the side effects from **immunotherapy** can be effectively prevented or managed. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking an **immunotherapy**.

For further information and advice on **immunotherapy** side effects, see ESMO's patient guide on **immunotherapy**-related side effects and their management (<https://www.esmo.org/for-patients/patient-guides/immunotherapy-side-effects>).



Long-term side effects

After completing treatment for **HCC**, you may experience some long-term side effects, depending on the treatment you have received.

After a liver transplant, a small number of patients experience chronic liver rejection, in which the body begins to reject the new liver around a year after transplant. This can be treated with anti-rejection medicines, but some patients will need to have another liver transplant.

Radiotherapy can have side effects that gradually appear over a long time, including bowel changes and diarrhoea, abdominal pain and permanent skin changes in the treatment area. It is important that you let your doctor or nurse know about any new side effects that you are experiencing, even if they occur months or years after the **radiotherapy** treatment.

The long-term effects of **HCC** and its treatment can have a negative effect on both physical and mental quality of life, so it is important that you tell your doctor or nurse about any persistent or new symptoms. Your doctor or nurse will also work with you to develop a personalised survivorship care plan.

For further information and advice regarding how to regain your life as far as possible after treatment for cancer, see ESMO's patient guide on survivorship (<https://www.esmo.org/for-patients/patient-guides/survivorship>).



What happens next?

Follow-up appointments

You will be able to discuss any concerns you have at your follow-up appointments

After treatment for **HCC**, your doctor will arrange follow-up appointments to ensure that any **recurrences** or long-term side effects are diagnosed and treated quickly.

Your doctor will let you know how often you need to return for further follow-up appointments, but a typical follow-up schedule after **curative** treatment would involve check-ups every 3 months in the first year after treatment, and every 6 months thereafter (*Vogel et al., 2018*). During these appointments, you may have a clinical examination, blood tests and a **CT** or **MRI** scan.



What if I need more treatment?

Despite the best possible treatment at diagnosis, there is a possibility that your cancer may return. Cancer that comes back is called a **recurrence**. The treatment that you will be offered depends on the extent of the **recurrence**, your previous treatment and your overall health. Your doctor will discuss all of the treatment options with you.

Looking after your health

After you have had treatment for **HCC**, you may feel very tired and emotional. Give your body time to recover and make sure you get enough rest, but there is no reason to limit activities if you are feeling well. It is important to take good care of yourself and get the support that you need.

- **Take plenty of rest when you need it:** Give your body time to recover. Complementary therapies, such as aromatherapy, may help you relax and cope better with side effects. Your hospital may offer complementary therapy; ask your doctor for details.
- **Eat well and keep active:** Eating a healthy diet and keeping active can help improve your fitness. It is important to start slowly and build up as you start to feel better.

The following eight recommendations form a good foundation for a healthy lifestyle after cancer

(Wolin *et al.*, 2013):

- Don't smoke.
- Avoid second-hand smoke.
- Exercise regularly.
- Avoid weight gain.
- Eat a healthy diet.
- Don't drink alcohol at all.
- Stay connected with friends, family and other cancer survivors.
- Attend regular check-ups and screening tests.



A healthy, active lifestyle will help you to recover physically and mentally

Regular exercise is an important part of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. It is very important that you listen carefully to the recommendations of your doctor or nurse, and talk to them about any difficulties you have with exercise.

Emotional support

It is common to be overwhelmed by your feelings when you have been diagnosed with cancer and when you have been through treatment. If you feel anxious or depressed, talk to your doctor or nurse – they can refer you to a specialist counsellor or psychologist who has experience of dealing with the emotional problems of people coping with cancer. It may also help to join a support group so that you can talk to other people who understand exactly what you are going through.



Support groups

In Europe, there are patient advocacy groups, which help patients and their families to navigate the **HCC** landscape. They can be local, national or international, and they work to ensure patients receive appropriate and timely care and education. These groups can provide you with the tools you may need to help you better understand your disease, and to learn how to cope with it, living the best quality of life that you can.

The European Liver Patients' Association (ELPA) is a platform that brings together patient groups to promote the interests of people with liver disease. It was established in 2005 and works to increase awareness of liver disease and encourage collaboration with professional bodies. For further information about ELPA visit: <https://elpa.eu>.



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GLOSSARY

AFLATOXIN

A harmful substance made by certain types of mould that is often found on poorly stored grains and nuts

ALOPECIA

Hair loss

ALPHA FETOPROTEIN (AFP)

A protein normally produced by a foetus. An elevated level of **AFP** can suggest the presence of liver cancer

ANGIOSARCOMA

A type of cancer that begins in the cells that line blood vessels or lymph vessels

ANTI-HYPERTENSIVE (TREATMENT)

A type of drug used to treat high blood pressure

ATEZOLIZUMAB

A type of **immunotherapy** that blocks a protein called PD-L1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

BARCELONA CLINIC LIVER CANCER (BCLC)

A staging system for liver cancer based on the number and size of **tumours**, the spread of the cancer, overall health and liver function

BEVACIZUMAB

A type of **targeted therapy** used to treat some cancers. It is a monoclonal antibody that targets vascular endothelial growth factor and prevents the cancer cells from developing their own blood supply, thus helping to slow down **tumour** growth

BILE

A fluid made by the liver and stored in the **gallbladder**. **Bile** helps to digest fat when released into the small intestine

BILE DUCT

Tube through which **bile** passes from the liver and **gallbladder** to the small intestine

BIOMARKER

Biological molecule found in tissue, blood or other body fluids that is a sign of a condition or disease, or describes the behaviour of the disease

BIOPSY

A medical procedure in which a small sample of cells or tissue is taken for examination under a microscope

BLOOD TRANSFUSION

A procedure in which whole blood or parts of blood are put into a patient's bloodstream through a vein

CABOZANTINIB

A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells, causing them to die. It is administered as a once-daily tablet

CATHETER

A flexible tube used to deliver fluids into or withdraw fluids from the body

CHEMOTHERAPY

A type of cancer treatment using medicine that kills the cancer cells by damaging them, so that they cannot reproduce and spread

CHOLANGIOCARCINOMA

Cancer that develops in the **bile ducts** (also known as **bile duct** cancer)

CISPLATIN

A type of **chemotherapy** that is used in **TACE**

CLINICAL TRIAL

A study that compares the effects of one treatment with another

COMPUTED TOMOGRAPHY (CT)

A scan using **x-rays** and a computer to create detailed images of the inside of your body

CURATIVE (TREATMENT)

A treatment that is intended to cure the cancer

DEOXYRIBOSE NUCLEIC ACID (DNA)

The chemical that carries genetic information in the cells of your body

DIABETES

A condition in which the kidneys make a large amount of urine. Usually refers to diabetes mellitus in which there is a high level of sugar in the blood

DIALYSIS

A process by which blood is filtered to remove waste products and excess fluid from the body when the kidneys are not working properly

DIETICIAN

A qualified health professional who is an expert on diet and nutrition

GLOSSARY

DOXORUBICIN

A type of **chemotherapy** that is used in **TACE**

DYSPNOEA

Shortness of breath

END-STAGE (LIVER FUNCTION)

Chronic liver failure

FATIGUE

Overwhelming tiredness

FIBROLAMELLAR CARCINOMA

A rare type of **HCC** that typically affects young adults

FIRST-LINE (TREATMENT)

The initial treatment(s) given to a patient

GALLBLADDER

An organ located below the liver, which stores **bile**

GASTROINTESTINAL SYSTEM

The system of organs responsible for getting food into and out of the body and for making use of food to keep the body healthy – includes the oesophagus, stomach and intestines

HAND-FOOT SYNDROME

A condition marked by pain, swelling, numbness, tingling or redness of the hands or feet. It sometimes occurs as a side effect of certain anti-cancer drugs

HEPATITIS B VIRUS (HBV)

A virus that causes inflammation of the liver

HEPATITIS C VIRUS (HCV)

A virus that causes inflammation of the liver

HEPATOBLASTOMA

A type of liver cancer that occurs in children

HEPATOCELLULAR CARCINOMA (HCC)

The most common type of liver cancer. Develops in **hepatocytes**

HEPATOCTES

Liver cells

HIGH DOSE RATE (HDR) BRACHYTHERAPY

A type of **radiotherapy** in which a **tumour** is subjected to a high dose of **ionising radiation** by placement of a radioactive material directly inside or next to the **tumour**

HYPERTENSION

Abnormally high blood pressure

IMMUNOTHERAPY

A type of cancer treatment that stimulates the body's immune system to fight the cancer

IONISING RADIATION

Any type of particle or electromagnetic wave that carries enough energy to ionise or remove electrons from an atom (e.g. **x-rays**)

JAUNDICE

A condition in which the skin and the whites of the eyes become yellow, urine darkens and stools becomes lighter than normal. Occurs when the liver is not working properly or a **bile duct** is blocked

LAPAROSCOPY

A procedure that involves the insertion of a thin, tube-like instrument with a light and a lens for viewing (laparoscope) through the abdominal wall to examine the inside of the abdomen and/or remove tissue

LENVATINIB

A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells, causing them to die. It is administered as a once-daily tablet

LEUKOPENIA

A decrease in the number of leukocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

LIVER CIRRHOSIS

A chronic, progressive disease in which liver cells are replaced by scar tissue

LYMPH NODES

Small structures throughout the **lymphatic system** that work as filters for harmful substances, such as cancer cells or bacteria

LYMPHATIC SYSTEM

A network of tissues and organs that help rid the body of toxins, waste and other unwanted materials. The primary function of the **lymphatic system** is to transport lymph, a fluid containing infection-fighting white blood cells, throughout the body

GLOSSARY

MAGNETIC RESONANCE IMAGING (MRI)

A type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body

MARGIN

The edge or border of the tissue removed in cancer surgery. The **margin** is described as negative or clean when no cancer cells are found at the edge of the tissue, suggesting that all of the cancer has been removed. The **margin** is described as positive or involved when cancer cells are found at the edge of the tissue, suggesting that all of the cancer has not been removed

MICROWAVE ABLATION

A form of **thermal tumour ablation** in which microwaves create heat to destroy a **tumour**

MULTIDISCIPLINARY TEAM

A group of healthcare workers who are members of different disciplines (e.g. oncologist, nurse specialist, physiotherapist, radiologist) and provide specific services to the patient. The activities of the team are brought together using a care plan

NEUTROPENIA

An abnormally low level of **neutrophils** in the blood which increases the risk of infection

NEUTROPHIL

A type of white blood cell that plays an important role in fighting off infection

NIKOLUMAB

A type of **immunotherapy** that blocks a protein called PD-1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in the arm or chest

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

A type of liver disease caused by a build-up of fat in the liver, which usually affects people who are overweight. **NAFLD** can lead to serious liver damage, including **liver cirrhosis**

NON-ALCOHOLIC STEATOHEPATITIS (NASH)

A serious form of **NAFLD**, in which the liver becomes inflamed

PALLIATIVE (CARE)

The care of patients with advanced, progressive illness. It focuses on providing relief from pain, symptoms and physical and emotional stress, without dealing with the cause of the condition

PEMBROLIZUMAB

A type of **immunotherapy** that blocks a protein called PD-1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in the arm or chest

PERCUTANEOUS

Passing through the skin

PERFORMANCE STATUS

A measure of how well a patient can carry out ordinary daily activities

PORTAL VEIN

A blood vessel that carries blood to the liver from the intestines, spleen, pancreas and **gallbladder**

PROGNOSIS

The likely outcome of a medical condition

PRURITUS

Severe itching of the skin

RADIOFREQUENCY ABLATION

A form of **thermal tumour ablation** in which a high-frequency electric current creates heat to destroy a **tumour**

RADIOTHERAPY

Treatment involving the use of high-energy radiation, which is commonly used to treat cancer

RAMUCIRUMAB

A type of **targeted therapy** that blocks the action of a protein called vascular endothelial growth factor, and prevents the cancer cells from developing their own blood supply, thus helping to slow down **tumour** growth. It is administered through a drip into a vein in the arm or chest

RECURRENCE

Return of a cancer

GLOSSARY

REGORAFENIB

A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells, causing them to die. It is administered as a once-daily tablet for 3 of every 4 weeks

RESECTION

Surgery to remove tissue

RISK FACTOR

Something that increases the chance of developing a disease

SECOND-LINE (TREATMENT)

Subsequent treatments given to a patient once the previous therapy has not worked or has been stopped because of the occurrence of side effects or other concerns

SELECTIVE INTERNAL RADIOTHERAPY (SIRT)

A type of **radiotherapy** in which radioactive microspheres are injected into the blood vessels supplying the liver. These microspheres damage the **tumour** and the blood vessels it needs to survive

SORAFENIB

A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells, causing them to die. It is administered as a once-daily tablet

STEREOTACTIC BODY RADIOTHERAPY (SBRT)

A type of external **radiotherapy** that uses special equipment to position the patient and precisely deliver radiation to a **tumour**

STEROID

A type of drug used to relieve swelling and inflammation. Some **steroid** drugs also have anti-**tumour** effects

STOMATITIS

Inflammation of the inside of the mouth

TARGETED THERAPY

A type of cancer treatment that uses drugs or other substances to precisely identify and attack cancer cells, usually while doing little damage to normal cells

THERMAL TUMOUR ABLATION

A procedure using heat to destroy a **tumour**

TRANSARTERIAL CHEMOEMBOLISATION (TACE)

A procedure in which the blood supply to a **tumour** is blocked after **chemotherapy** is administered in blood vessels near the **tumour**

TUMOUR

A lump or growth of abnormal cells. **Tumours** may be benign (not cancerous) or malignant (cancerous). In this guide, the term '**tumour**' refers to a cancerous growth, unless otherwise stated

TYROSINE KINASE INHIBITOR

A type of **targeted therapy** that inhibits tyrosine kinases, which are substances that send growth signals to cells

ULTRASOUND

A type of medical scan where sound waves are converted into images by a computer

X-RAY

An imaging test, using a type of radiation that can pass through the body, which allows your doctor to see images of inside your body

Hepatocellular Carcinoma

This guide has been prepared to help you, your friends and your family better understand the nature of hepatocellular carcinoma and the treatments that are available. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of hepatocellular carcinoma. We recommend that you ask your doctor about the tests and types of treatments available in your country for your stage of hepatocellular carcinoma.

This guide has been written by Kstorfin Medical Communications Ltd on behalf of ESMO.

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We can help you understand hepatocellular carcinoma and the available treatment options.

The ESMO Guides for Patients are designed to assist patients, their relatives and caregivers to understand the nature of different types of cancer and evaluate the best available treatment choices. The medical information described in the Guides for Patients is based on the ESMO Clinical Practice Guidelines, which are designed to guide medical oncologists in the diagnosis, follow-up and treatment in different cancer types.

For more information, please visit www.esmo.org

