



# INVESTIGATING A NEW APPROACH TO POST-SURGICAL CARE FOR PATIENTS WITH COLON CANCER

# WHAT IS SAGITTARIUS?

**SAGITTARIUS IS A CLINICAL STUDY THAT COULD HELP TO DEMONSTRATE THE BENEFITS OF A NEW APPROACH TO TESTING AND TREATING PATIENTS WITH COLON CANCER TO REDUCE THE RISK OF RECURRENCE AFTER SURGERY.**

The study is for patients with either:



## High-risk stage II colon cancer

(cancer that has crossed the colon intestine wall).



## Stage III colon cancer

(cancer that has spread to neighbouring lymph nodes. If someone is found to have cancer in their lymph nodes, it's usually a sign that the cancer has or will soon spread to other parts of the body).

Patients with high-risk stage II or stage III colon cancer usually receive surgery with the aim of completely removing the cancer and providing a cure. However, sometimes a few cancer cells may remain in the body (known as minimal residual disease (MRD)), which means the cancer is more likely to come back.

SAGITTARIUS will assess the use of liquid biopsy (a simple type of blood test) to detect signs of cancer in patients after they have had surgery. The results from the liquid biopsy will be used to guide the post-surgical treatment of patients with high-risk stage II and stage III colon cancer. This personalised approach will be compared with the standard, one-size-fits-all treatment pathway that patients at these stages of disease generally follow.

It is hoped that, once the efficacy of this new approach is proven, the method used in SAGITTARIUS will ensure patients receive the right treatment at the right time, avoid unnecessary treatments and side effects, and improve post-surgical care and out-comes for patients with colon cancer.



## WHAT IS THE **AIM OF THE STUDY?**

The aim of the SAGITTARIUS study is to assess whether the use of liquid biopsy detection to personalise post-surgical care is superior/equal to the effectiveness of conventional treatment pathways, and if it can result in fewer side-effects.

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## WHY SHOULD I **TAKE PART?**

Your participation might be beneficial to your health, as you might receive a treatment that is more suited to your specific case after surgery, and you may avoid unnecessary treatments and the side effects that are associated with them.

Your participation will also aid in the success of the SAGITTARIUS project, by contributing knowledge that can be used to design, plan, and implement appropriate post-surgical care for patients with colon cancer across the EU.

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## WHAT IS **COLON CANCER?**

Colon cancer, also known as bowel cancer, develops in the colon (the large bowel or the large intestine). In Europe, it is the second most common cancer with more than **500,000 European citizens diagnosed every year**. The good news is that colon cancer is highly treatable if diagnosed in its early stages.

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## WHAT IS HIGH-RISK **STAGE II** AND **STAGE III COLON CANCER?**

Staging is a way of describing the size of a cancer and how far it has grown or spread. When doctors first diagnose a cancer, they carry out tests to check how big the cancer is, whether it has spread into surrounding tissues, and whether it has spread to other parts of the body.

For most cancers, the stage is a Roman numeral from 0 to IV, where stage 0 is the lowest and IV (4) is the highest. As a rule, the lower the number, the less the cancer has spread. Staging is important because it helps your doctors to know which treatments would be best for you.

The different stages of colon and rectal (collectively known as colorectal) cancer are below.



STAGE	LOCATION
STAGE 0	The cancer has not grown beyond the first layer of the colocteral wall, it is non-invasive cancer.
STAGE I	The cancer has grown into either second or third layer of the colocteral wall, but there is no cancer nearby or distant sites
STAGE II	The cancer has grown into the fourth layer of or the outside of the colorectal wall; there is no cancer nearby or distant sites.
STAGE III	the cancer has spreas from the colorectal to nearby lymph nodes or there are small secondary tumours within the colorectal
STAGE IV	The cancer has spread to distant organs as the liver or lungs.

**Stage II** colon cancer indicates that the tumour has grown into the outer layer of the intestine wall.

**High Risk Stage II** colon cancer indicates that the tumour has grown through the outer layer of the intestine wall. This is called 'High Risk' because there is a higher risk that small cancer cells may have spread to other parts of the body having escaped the tumour through the blood and lymph system.

**Stage III** Colon Cancer indicates that the cancer has definitely escaped the tumour and is already been found in local tissues, e.g. lymph nodes.

## WHAT IS **THE GOAL OF SURGERY** FOR COLON CANCER?

The goal of surgery in earlier stage colon cancer is usually to completely remove the cancer, with the aim of providing a cure.

Surgery with curative intent is generally the first treatment option for high-risk stage II and stage III patients.

Unfortunately, in around half of these patients, the disease may come back in two to three years following surgery, due to traces of cancer that remain in the body after surgery, known as minimal residual disease (MRD). Until now, patients with MRD have been indistinguishable from those without, as MRD is invisible on CT or MRI scans because the cancer cells are too small.

That is why doctors generally suggest that all patients have chemotherapy after surgery to destroy any small cancer cells that may have escaped into the body.



# WHAT NORMALLY HAPPENS **AFTER COLON CANCER SURGERY?**

Normally, after surgery, the patient's doctor will discuss the various options with patients, and they will make a decision together.

For people with high-risk stage II or stage III colon cancer, chemotherapy is usually recommended soon after recovery from surgery.

The purpose of giving chemotherapy after surgery is to remove any traces of cancer that may be remaining in the body (known as minimal residual disease (MRD)) to stop the cancer from coming back. Currently, all patients with high-risk stage II or stage III colon cancer indiscriminately receive chemotherapy after surgery because, until now, it has not been possible to know who is at risk of having minimal residual disease and who is not. But the SAGITTARIUS study may change all of that.

Chemotherapy treatment after surgery is called 'adjuvant' chemotherapy. Amongst patients and oncologists, this kind of adjuvant treatment is also known as 'mop-up' chemotherapy because it is intended to mop up any remaining microscopic cancer cells floating around the body.

## WHAT WILL HAPPEN AFTER **COLON CANCER SURGERY IN THE SAGITTARIUS STUDY?**

People participating in the SAGITTARIUS study will be tested 3-5 weeks after surgery via a new test called liquid biopsy.

A liquid biopsy is a simple kind of blood test that detects cancer DNA that is circulating in the blood, called "circulating tumour DNA" or "ctDNA." ctDNA is DNA released by the tumour cells into the blood and therefore it carries the same characteristics as the tumour of origin. ctDNA has been shown to be a strong indicator that cancer cells remain in the body (Minimal Residual Disease).<sup>1,2,3</sup> If the liquid biopsy test is positive, it means that there might be other cancer cells somewhere in the body, even though the primary tumour has been removed.



### References:

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2. Siravegna G, Mussolin B, Venesio T, Marsoni S, Seoane J, Dive C, Papadopoulos N, Kopetz S, Corcoran RB, Siu LL, Bardelli A. How liquid biopsies can change clinical practice in oncology. *Ann Oncol*. 2019. 30(10): p. 1580-1590. doi: 10.1093/annonc/mdz227. PMID: 31373349
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The genetic profile of the primary tumour will be analysed and then used to create a tailor-made liquid biopsy test for each patient participating in SAGITTARIUS. This liquid biopsy will then be able to detect tumour DNA in their blood. This will help doctors understand which personalised treatment strategies should be used.

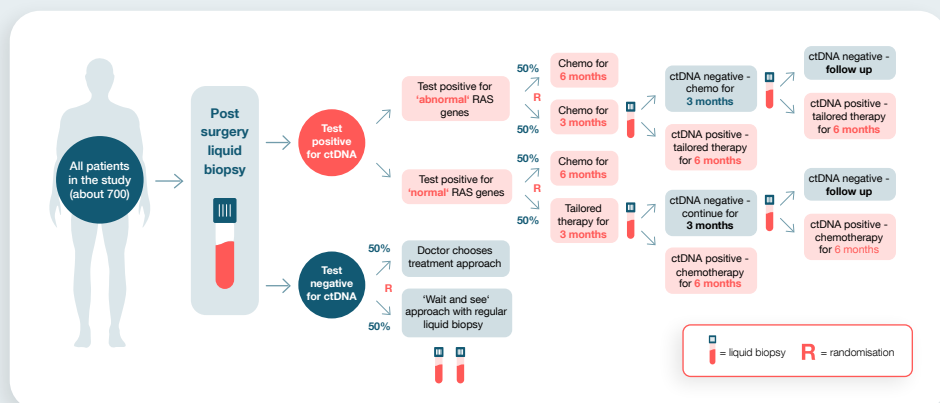
Liquid biopsy is a technique used for research and is not yet considered a diagnostic test. Thus, the SAGITTARIUS approach is still experimental. It must be evaluated and compared to the standard approach before entering the clinical routine. For this reason, one-half of the patients participating in SAGITTARIUS will experience the new customised pathway (experimental), while the other half will continue to receive the standard adjuvant chemotherapy. The assignment of each patient to one of the two pathways (experimental or conventional) will be done by an assignment process by chance called 'randomisation' (R).

Participants will be tested via liquid biopsy several times throughout the study to assess the presence of ctDNA in the blood, thus monitoring the evolution of the disease, and the response to treatments. The type of treatment given to participants may then change depending on the results of subsequent liquid biopsies.

You may be tested several times with liquid biopsy to check for any ctDNA in your blood at time and treatment progresses. If there are any signs of ctDNA, your doctors will prescribe an alternative treatment to increase the possibility for your cancer to be definitely removed.

## WHAT DOES **LIQUID BIOPSY INVOLVE?**

A liquid biopsy test involves a simple blood test. A healthcare professional will take a blood sample in the normal way, usually from a vein in your arm. The blood sample will be sent to a lab for testing.



# WHAT WILL THE LIQUID BIOPSY REVEAL AND WHAT TREATMENT WILL I BE GIVEN?

The diagram below shows the different treatment journeys that participants in the study will go through. After the initial post-surgery liquid biopsy, the participants will be split into two groups depending on the result – those who test positive for ctDNA, and those who test negative.

If your blood contains circulating tumour DNA (ctDNA), you will be assigned by randomisation to either the group receiving the conventional chemotherapy or the one receiving a personalised therapy. In the second group, the personalised therapy will depend on the molecular characteristics of the tumour.

Some patients will have certain genetic “biomarkers”, which show they will respond well to certain treatments. Biomarkers are specific molecules, genes, or characteristics within a patient’s tumour that provide valuable information about the cancer’s behaviour and how well it is likely to respond to particular treatments.

The analysis of the surgical tumour samples will reveal these features and the unique genetic profile of each patient, and it will guide the personalised treatment choice.

You may be tested several times with liquid biopsy to check for any ctDNA in your blood at time and treatment progresses. If there are any signs of ctDNA, your doctors will prescribe an alternative treatment to increase the possibility for your cancer to be definitely removed.

If you test negative for ctDNA, you will be assigned by randomisation to either the group undergoing a “wait and see” approach, with subsequent liquid biopsy tests to check if there is any ctDNA in your blood as time progresses, or the group receiving conventional adjuvant treatment according to your physician’s choice. You will be tested several times with liquid biopsy to check for any ctDNA in your blood. If at any time there are any signs of ctDNA, a therapy will be prescribed, depending on the molecular profile of your tumour.



The type of treatment you receive will either be:



### CHEMOTHERAPY

Chemotherapy uses medicines to eradicate cancer cells. In high-risk stage II or stage III colon cancer, it is given after surgery to eliminate any cancer cells that may have been left behind (known as adjuvant chemotherapy). Chemotherapy is given orally (via tablets) or intravenously (into a vein). As with every medicine, it may cause unpleasant side effects, including tiredness, nausea and hair loss. These may be controlled with medicines and usually go away once treatment has finished. Unfortunately, in a few cases, it may also have serious side effects, such as damaging or causing peripheral nerve dysfunction (called peripheral sensory neuropathy), which is usually reversible but permanent in some patients for reasons as yet unknown.



### TARGETED THERAPY

Targeted therapy targets specific molecules in the tumour, usually with the aim of blocking the growth and spread of cancer cells, while limiting damage to healthy cells.



### IMMUNOTHERAPY

Immunotherapies are designed to boost the body's own immune system to help fight cancer. Unfortunately, in colon cancer only a minority of patients with specific tumour molecular traits respond to immunotherapy.

## WHAT IF I GET ASSIGNED TO THE STANDARD TREATMENT GROUP? WON'T I RECEIVE WORSE TREATMENT?

The new customised pathway being assessed in SAGITTARIUS is experimental, and nobody knows for certain whether it will be better than the standard approach. There are pros and cons to being in either group.

If you are in the standard group, you will receive treatment that has been used for many years and is proven to be effective. One consequence of the standard treatment is the risk of overtreatment. A proportion of High-Risk Stage II or Stage III patients will not have any cancer cells in their body, yet still suffer the impact of the chemotherapy side-effects.

Alternatively, if there are cancer cells present, the treatment will not be personalised to the genetic profile of the tumour.

The pros to being in the experimental group are that you might receive a treatment that is more suited to your specific case after surgery, and you may avoid unnecessary treatments and the side effects that are associated with them. The cons are that this is an experimental approach. Liquid biopsy is not yet a validated clinical diagnostic tool. There is the possibility that some minimal residual disease could be undetected by the liquid biopsy.



This is why we need to run the clinical trial – to properly assess whether liquid biopsy can be a validated clinical diagnostic tool. This will reduce the number of people being unnecessarily treated (overtreated) when they do not need it. Conversely it will confirm the necessity of treatment for those who do have minimal residual disease.

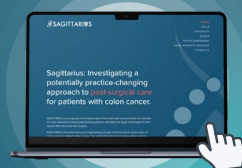
It will also monitor the progress of the treatment and identify the need for changes. It will increase the opportunity for patients to receive the most appropriate treatment for their tumour type.

## WHAT CAN I DO TO **MAXIMISE MY HEALTH DURING THE STUDY?**

Even when you are receiving treatment for colon cancer, there are steps you can take to maximise your health. In particular, diet, exercise, and lifestyle play important roles in improving outcomes in colon cancer. For example, it has been shown that patients with stage III colon cancer who followed nutrition and physical activity guidelines survived significantly longer than those who did not.<sup>4</sup>

**You can find out more information about the importance of diet, nutrition, and physical activity for people with colon cancer in this World Cancer Research Fund report:**

YOU CAN FIND **MORE INFORMATION** ON  
<http://sagittarius-horizon.eu>



[www.wcrf.org/wp-content/uploads/2021/02/Colorectal-cancer-report.pdf](http://www.wcrf.org/wp-content/uploads/2021/02/Colorectal-cancer-report.pdf)



### **EAT A HEALTHY DIET AND LIMIT RED AND PROCESSED MEATS.**

If you eat red meat, limit consumption to no more than about three portions per week. Three portions are equivalent to about 350–500g (about 12–18oz) cooked weight. Consume very little, if any, processed meat, such as bacon, sausages and processed sandwich meat. Eating healthy and unprocessed or limited processed foods, including plenty of fruits, vegetables, and whole grains, limiting red and processed meats and sugary drinks, lowers the overall risk of colorectal cancer. Eating whole grains plus eating 5 or more daily servings of fruits and vegetables appears to lead to improved colon cancer survival.<sup>4</sup>

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In addition, it has been shown that eating frequent small meals will ensure your body is getting enough calories, protein, and nutrients to tolerate treatment. Eating a varied diet containing these elements can help you to cope with treatment side effects, handle the best dose of certain treatments to treat your cancer, recover and heal faster, fight off infections, and feel less fatigued, stronger, healthier and have more energy.<sup>5</sup>

In fact, nutrition is so important in colon cancer – for prevention of further issues and to help with treatment and recovery – that it is advisable to search for a nutritionist with expertise in colon cancer to provide you with the tailored support that you need.



### **MAINTAIN A HEALTHY WEIGHT.**

Aside from overall impact on general health and wellbeing, obesity is known to be a risk factor for both cancer incidence and recurrence.<sup>6</sup> Therefore, promoting weight loss is an ideal target for those living with and beyond a cancer diagnosis. If you are overweight, a good starting point can be to try to stop gaining weight, which has health benefits by itself. Then, for a bigger health boost, slowly work to lose some weight over time.



### **EXERCISE TO STRENGTHEN YOUR MUSCLES.**

Try to be physically active several times a week. Physical exercises are key to preventing muscle mass loss and maintaining functionality and physical activity. Exercise has been shown to improve many side effects stemming from cancer and its treatments, as well as improving quality of life.<sup>7</sup>



### **LIMIT ALCOHOL AND TOBACCO USE.**

During treatment, drinking alcohol or using tobacco can make side effects worse. They are also major risk factors for most types of cancer. You should refrain from smoking and limit alcohol intake during cancer treatment of any kind before, during and after cancer treatment.



### **SEEK MENTAL HEALTH OR EMOTIONAL SUPPORT IF NEEDED.**

If you are struggling with your cancer diagnosis or your treatment, do reach out for help. You may need counselling or other kind of emotional or psychological support. Receiving psychological support and learning coping strategies have been shown to reduce distress, depression and anxiety in patients diagnosed with colon cancer, improving their quality of life.<sup>8</sup> Please do seek help if you need it. Your doctor is a good place to start.

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## WHAT IF I HAVE **OTHER QUESTIONS?**

If you have any questions related to the study, or more generally about colon cancer, you can ask your treating doctor or other healthcare professionals at your treating hospital.

# Glossary

**Adjuvant therapy:** Treatment given after the main treatment to reduce the chance of cancer coming back by destroying any remaining cancer cells. It usually refers to chemotherapy.

**Biomarkers:** Specific molecules, genes, or characteristics within a patient's tumour that provide valuable information about the cancer's behaviour and how susceptible it is to certain treatments. The tissue taken during surgery can be tested to identify some of these molecular biomarkers.

**ctDNA (circulating tumour DNA):** DNA that comes from a small fraction of tumour cells disseminated from the primary colon cancer to other parts of the body (mostly in the liver) and that is circulating in the blood. It shares the same characteristics as the tumour of origin, which can give doctors essential information to help treatment decisions.

**High-risk stage II colon cancer:** A colon cancer that crossed the colon intestine wall. Doctors have a list of criteria to reach this diagnosis.

**Liquid biopsy:** A blood test that detects DNA in the blood, called "circulating tumour DNA" or "ctDNA".

**MRD (minimal residual disease):** A term used to describe the small number of cancer cells left in the body after cancer treatment, such as surgery.

**Randomisation:** The process of assigning participants in a study to different treatment groups. Each participant has an equal chance of being assigned to any group.

**Stage III colon cancer:** A colon cancer where the cancer has spread to the nearby area, including the lymph nodes.



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