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SAGITTARIUS

First 6 patients involved in the SAGITTARIUS clinical trial, for a personalised colon cancer therapy

November 2024

The SAGITTARIUS project, supported by the European Union's Horizon Europe programme, has already **recruited its first 6 patients**, marking the start of a clinical trial that could **transform colon cancer treatment globally**. Liquid biopsy, an **innovative precision medicine approach**, will be used in the study. The aim is to provide patients undergoing surgery for locoregional colon cancer (high-risk stage II and operable stage III) with a therapy that is more targeted at the molecular characteristics of their disease. In this way, the results obtained by SAGITTARIUS could help to improve the effectiveness of treatments for this type of cancer, together with the quality of life of patients and health costs compared to today.

"The participation of the first 6 patients marks the beginning of a path that could lead to new and better treatment options for millions. **This is just the first step towards results that could radically change the quality of life of colon cancer patients**," commented Silvia Marsoni (IFOM), scientific coordinator of the project, involving 7 partners in 5 European countries and a **network of over 20 clinical centres** in Italy, Spain and Germany.

The SAGITTARIUS project is coordinated and sponsored by the **Institute of Molecular Oncology - IFOM** (Italy), in collaboration with the **AIRC Foundation for Cancer Research** (Italy), the **Hospital del Mar Research Institute in Barcelona** (Spain), the **Bocconi University** (Italy), the **Digestive Cancers Europe** (Belgium), **SporeData OU** (Estonia), the **Vall d'Hebron Institute of Oncology - VHIO** (Spain) and the Berlin **Charité University Hospital - Universitätsmedizin** (Germany).

Special mention should be made of the **Niguarda Hospital**, which is part of the SAGITTARIUS clinical network and will be among the first to involve patients who will join the trial. An important task, since "in the Lombardy Region the annual estimated cases of colorectal cancer are about 7,000. Niguarda Hospital, which coordinates the Italian centres participating in SAGITTARIUS and with the Niguarda Oncology Foundation contributes to the supply of experimental drugs for this research, is once again at the forefront of providing timely, post-surgical care options for people with colon cancer," said Salvatore Siena, Head of Oncology at the Niguarda Hospital and Professor of Oncology at the University of Milan.

How can SAGITTARIUS make a difference?

Colon cancers, together with rectal cancers, account for around 10% of all cancer cases worldwide. In Italy alone, more than 50,000 new cases of these types of cancer are diagnosed every year.

Currently, the main treatment for patients with **locoregional colon cancer** is surgery to remove the tumour. However, sometimes it is not enough. Depending on the biological characteristics, the tumour may present micrometastases which are **not removed by surgery and therefore require further treatment**. These micrometastases are so small that they cannot be detected by radiological examinations, and this is why many patients after surgery is also submitted to post-operative chemotherapy (called adjuvant chemotherapy), to eliminate any remaining cancer cells. However, **this therapy may be unnecessary for people who do not have micrometastases, and avoiding it could save them from the toxicity of treatment**. Detecting the presence of micrometastases is therefore very important, and the liquid biopsy approach could play a leading role in this, as already demonstrated by many recent clinical studies. They include the PEGASUS clinical trial, supported by AIRC and sponsored by IFOM.

This is where **SAGITTARIUS** comes in. Using liquid biopsy to assess the presence or absence of micrometastases after surgery, the study aims to evaluate whether analyzing the characteristics of the tumours of colon cancer patients may help personalise the management and therapy of patients with high-risk stage II colon cancer and operable stage III colon cancer. The clinical trial will personalize treatments on two fronts: on the one hand, avoiding chemotherapy in those who may not need it, and on the other by replacing chemotherapy with other biological and immunological treatments based on the molecular characteristics of the tumour.

The SAGITTARIUS clinical trial: a precision medicine approach

The SAGITTARIUS study involves a network of 26 European clinical centres, and plans to recruit around 700-900 patients in Spain, Germany and Italy, under the expert guidance of Clara Montagut from the Hospital del Mar Research Institute (HMRIB), as the study coordinator. Elena Élez of the Vall d'Hebron Oncology Institute (VHIO), Sebastian Stintzing of the Charité Hospital (Charité - Universitätsmedizin Berlin) and Andrea Sartore-Bianchi (Niguarda Hospital in Milan and Università degli Studi di Milano) will be the clinical co-coordinators of the study, respectively for Spain, Germany and Italy, together with Salvatore Siena (Ospedale Niguarda di Milano and Università degli Studi di Milano) as principal investigators of the coordinating centre in Italy.

The main SAGITTARIUS tool will be the **liquid biopsy, an innovative test that detects the presence of tumour DNA in patients' blood**. The diagnostic use of this test in this set of patients is permitted for research purposes only and in clinical trials such as SAGITTARIUS. Although liquid biopsy is a valid and important tool for detecting the presence of micrometastases, it is not yet in clinical practice, but may soon be included in patient management guidelines.

After the surgical removal of colon cancer, any remaining cancer cells may release circulating tumour DNA (ctDNA) into the blood. These fragments retain some important features of the tumour from which they have been detached. Liquid biopsy allows this ctDNA to be detected. With individual tests for each patient, the SAGITTARIUS protocol should help identify the most appropriate postoperative treatment strategies for each patient and compare their effectiveness to standard therapy.

Patient involvement and study protocol

The first challenge of the SAGITTARIUS clinical trial is to **recruit 900 patients while meeting rigorous medical criteria and the schedule** which is needed to complete the tests for each patient's treatment assignment. **Patients should enter the study within 2-3 weeks after surgery**, which is only possible through close collaboration and coordination between surgeons and pathologists and medical oncologists in participating centres.

How will the clinical trial be conducted? First, each patient's tumour tissue will be analysed to **identify the tumour's "molecular signature"**. This will be used to **personalize the liquid biopsy test for each patient**, thus determining whether or not a micrometastatic disease is present.

If the test detects micrometastasis, patients will be randomly assigned to two groups: either the group receiving standard adjuvant chemotherapy or the group treated with customized therapies such as molecular target drugs or immunotherapy, based on the molecular characteristics of the tumour.

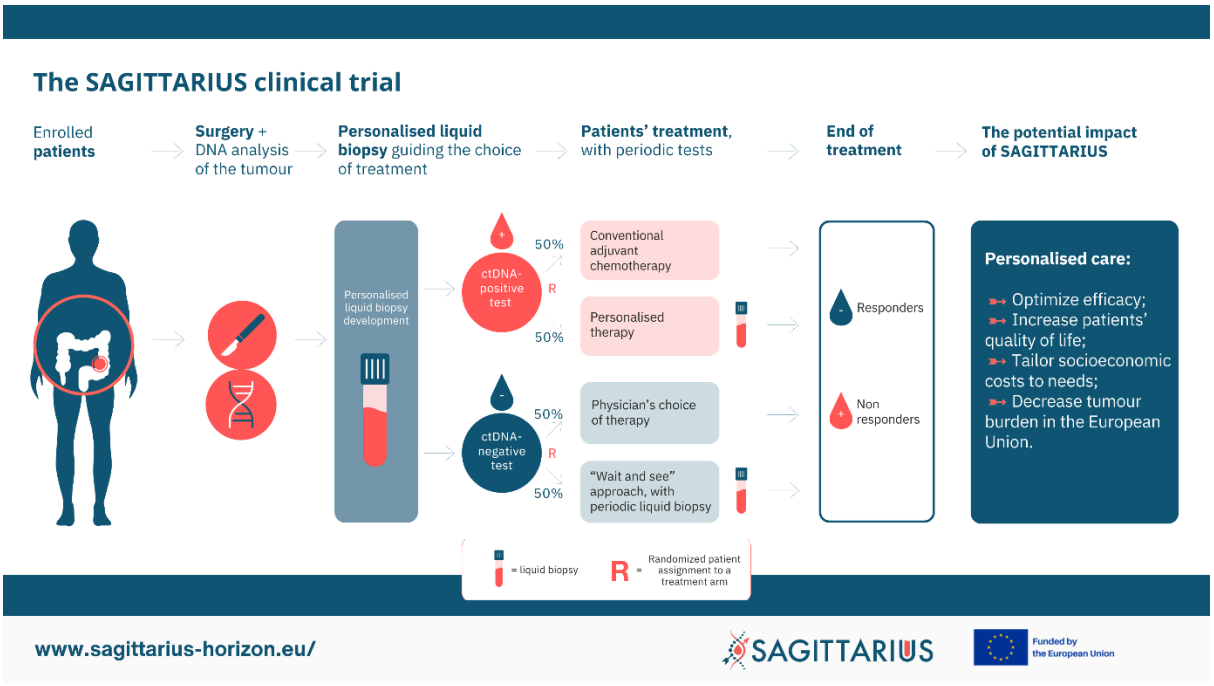
If micrometastases are absent, patients, potentially already treated by surgery, will be randomly divided into a group treated with mild therapies chosen by the doctor or the group with a "wait and see" approach, that is the patient's monitoring for 2 years after surgery without further treatment.

In any case, SAGITTARIUS experts will carry out periodic tests, adjusting treatments as necessary.

For more information

For further information or to participate in the trial, please contact: clinical.trials@ifom.eu.

Important news will also be published on the SAGITTARIUS website, in the newsletter and on social profiles: LinkedIn, Facebook, X, Instagram, YouTube.



More on the SAGITTARIUS project, partners, and clinical network

The SAGITTARIUS project includes partners and affiliated entities in 5 European countries: Italy, Belgium, Estonia, Spain and Germany.

- **IFOM**, the AIRC Institute of Molecular Oncology (Milan, Italy), under the guidance of Silvia Marsoni, coordinates the SAGITTARIUS project and its clinical trials;
- **Cogentech** (Milan, Italy), an affiliate partner of IFOM. In the person of Marco A. Pierotti, the company is responsible for the analysis of the genetic profile of tumours;
- The **AIRC Foundation for Cancer Research** (Milan, Italy), under the coordination of Cristina Zorzoli, is involved in stakeholder involvement and communication, dissemination and exploitation of project results;
- **Hospital del Mar Research Institute** (HMRIB), Barcelona (Spain), under the guidance of Clara Montagut. Responsible for the clinical trial and managing the Spanish clinical centres involved in the project;
- The **Research Centre for Health and Social Care Management** (CERGAS) of the Bocconi University in Milan (Italy), coordinated by Aleksandra Torbica and Carlo Baldassarre Federici, is responsible for the economic-health analysis aspects of the study;
- **Digestive Cancers Europe** (DiCE), Brussels (Belgium), coordinated by Zorana Maravic, Marianna Vitaloni and Natasha Münch. Together with AIRC, DiCE manages stakeholder engagement, communication and dissemination of SAGITTARIUS results; in addition, it is responsible for assessing the impact of the SAGITTARIUS approach on patient quality of life;
- **SporeData** OU, Tallinn (Estonia), is responsible for the integrative analysis of project data under the guidance of Ricardo Pietrobon;
- The **Vall d'Hebron Oncology Institute** (VHIO), Barcelona (Spain). Under the guidance of Elena Élez, VHIO is responsible for the clinical trial and is involved in cost-benefit analyses;
- The **Charité University Hospital** (Charité - Universitätsmedizin Berlin, Germany), under the direction of Sebastian Stintzing, is responsible for the clinical trial and coordinates the clinical trial in Germany.

The SAGITTARIUS clinical network

The participating oncology centres include:

For Italy:

- Ospedale Niguarda (Milan), Salvatore Siena e Andrea Sartore-Bianchi;
- Istituto Clinico Humanitas (Rozzano), Armando Santoro;
- Istituto Europeo di Oncologia (Milan), Maria Giulia Zampino;
- Fondazione Poliambulanza (Brescia), Michela Libertini;
- Azienda Unità Sanitaria Locale della Romagna (Ravenna), Stefano Tamberi;
- Ospedale Maggiore di Novara (Novara), Alessandra Gennari;
- Istituto di Candiolo (Candiolo), Elisabetta Fenocchio;
- Policlinico Universitario Gemelli (Rome), Lisa Salvatore;
- Azienda Ospedaliera Universitaria San Martino (Genova), Maria Stefania Sciallero;
- Azienda Ospedaliera Universitaria di Parma (Parma), Francesca Negri;
- Ospedale Santa Maria della Misericordia (Perugia), Mario Mandalà;
- Azienda Sanitaria Locale di Biella (Biella), Francesco Leone.

For Spain:

- Hospital del Mar (Barcelona), Clara Montagut;
- Hospital Vall d'Hebrón (Barcelona), Elena Élez;
- Hospital Sant Pau Barcelona (Barcelona), David Páez;

- Instituto Catalán de Oncologia (Barcelona), Cristina Santos;
- Hospital 12 de Octubre (Madrid), Cristina Graválos;
- Hospital Clinico Universitario San Carlos (Madrid), Javier Sastre;
- INCLIVA Instituto de Investigación Sanitaria (València), Noelia Tarazona;
- Hospital General Universitario de València (València), Maria José Safont;
- Hospital Universitario Marqués de Valdecilla (Santander, Cantabria), Carlos López;
- Hospital Universitario Reina Sofía (Córdoba), Enrique Aranda;
- Hospital Clínico Universitario de Santiago (Santiago de Compostela), Juan Ruiz;
- Hospital Universitario Miguel Servet (Zaragoza), Vicente Alonso;
- Complejo Hospitalario de Navarra (Navarra), Ruth Vera.

For Germany:

- Charité - Universitätsmedizin Berlin (Berlino), Sebastian Stintzing e Loredana Vecchione.

The facets of the SAGITTARIUS project

SAGITTARIUS is a project consisting of 4 interconnected sub-projects.

- The **SAGITTARIUS clinical trial** is a randomised clinical trial that compares the current standard of treatment, which is the same for all patients, with a personalised therapeutic approach based on the liquid biopsy results. The type of therapy of patients involved in the study is guided by the absence, presence or persistence of residual minimal disease (MRD), micrometastases, detected within 4 weeks of surgery by liquid biopsy. The SAGITTARIUS study will involve around 900 patients with high-risk stage II or operable III colon cancer in 26 centres in 3 countries (Italy, Spain and Germany).
- The **Health economics sub-project** will measure the direct and indirect cost implications of integrating liquid biopsy into clinical practice, clinical outcomes and broader social costs associated with colon cancer, including the impact on productivity and health workers. The SAGITTARIUS health economics assessment could allow for more cost-effective therapeutic approaches to be implemented in daily clinical practice.
- The **Quality of life sub-project** will analyse the impact of the SAGITTARIUS clinical approach on patients' quality of life.
- The **Omics sub-project**, funded separately, will carry out multi-omics analyses of patients' tumours, including RNA sequencing and single-cell analyses. The aim is to reveal the biological processes underlying tumour heterogeneity and why some are more likely than others to cause micrometastatic disease after surgery.

Clinical study coordinator centres

Ospedale Niguarda Cancer Center · Sistema Socio Sanitario Regione Lombardia · Oncologia Niguarda · Hospital del Mar Research Institute Barcelona · Charité

SAGITTARIUS consortium

IFOM · cogentech · AIRC · Hospital del Mar Research Institute Barcelona · Università Bocconi Milano · Digestive Cancers Europe · Spore Data · VHIO · Charité

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