

## Press Release

February 29<sup>th</sup>, 2024

# World Triple Negative Breast Cancer Day: innovation to cure more women

**World Triple Negative Breast Cancer Day, held on March 3<sup>rd</sup>, is a reminder that triple-negative breast cancers remain the most difficult to treat, and that only innovation and dynamic research can bring hope of curing more patients. At Institut Curie, Europe's leading breast cancer treatment center<sup>1</sup>, with its recognized expertise in fundamental, translational, and clinical research, several innovative trials are underway to develop new treatments and detect relapse at an early stage. These trials are part of the IHU "Institut des cancers des femmes" project founded by Institut Curie with PSL and Inserm.**

### SKYLINE

By unleashing certain capacities of the immune system, immunotherapy is a proven treatment for metastatic disease, but many patients still do not derive lasting benefit from it. Cancer uses many different mechanisms to evade treatment.

To reinforce the action of this immunotherapy, clinical researchers at Curie are proposing to **combine two immunotherapies targeting 2 different but complementary mechanisms**, PD-L1 and TIGIT, with atezolizumab and tiragolumab, in addition to chemotherapy. The first trial of its kind, Skyline is a Phase I/II trial that will evaluate the toxicity and anti-tumor activity of the combination of the two immunotherapies. Trial opening imminent.

### CUPCAKE

Institut Curie is one of the world leaders in the detection and analysis of circulating tumor DNA in patients' blood, a method that has proven its effectiveness in anticipating relapse and optimizing treatment. A vast multi-center study, called CUPCAKE, coordinated by Institut Curie, will evaluate the **value of liquid biopsy in predicting relapse** in triple-negative breast cancer in a large cohort. The aim is to be able to rapidly propose a therapeutic alternative, when relapse is limited both in size and number of metastases.

This study will evaluate the efficacy of combined monitoring of circulating DNA in the blood, measured every three months, and whole-body mapping of tumor involvement with a nuclear medicine approach - PET/CT using FAPI, a new tracer with better performance than conventional PET/CT for triple-negative cancers. Opening soon.

Among the 60,000 new cases of breast cancer diagnosed each year in France, **triple-negative breast cancer affects around 15% of patients**, representing 9,000 new cases detected each year.

Unresponsive to hormonal treatments and anti-HER2 targeted therapy, it is one of the most aggressive and difficult-to-treat breast cancers, with three-quarters of patients failing to respond to treatment.

It is often diagnosed in younger women (40% are under 40), with a higher risk of early metastatic recurrence and shorter overall survival than other breast cancer subtypes.

The biggest challenges in triple-negative breast cancer are:

- earlier detection and mapping of metastases,
- better prediction of efficacy and resistance to immunotherapy,
- development of new therapeutic options.

Source INCa 2023

<sup>1</sup> With over 7,000 women undergoing treatment and more than 3,000 new cases of breast cancer treated every year, the Institut Curie is Europe's leading breast cancer treatment center.

## TOPOLOGY

Many triple-negative breast cancers are characterized by defects in the DNA repair mechanisms at work during cell division. Agents that target these "defects" are therefore of particular interest. The TOPOLOGY study will **investigate the activity of one such treatment, the new agent PLX038, and ensure its safety and mechanism of action.**

This is a chemotherapy (SN38), already effective in these cancers, coupled with a kind of "vehicle" (PEG) that will enable the treatment to be delivered in a more concentrated form to the tissues and the tumor, while offering a longer release time. These two properties should make the molecule more effective, while guaranteeing controlled toxicity.

This is a Phase II study which, if successful, will lead to the launch of a larger-scale trial to compare this innovative agent with the reference treatment. The study has been open since the end of February 2024.

*The principal investigator for these 3 clinical trials is Prof. François-Clément Bidard, medical oncologist at Institut Curie and professor at the Université de Versailles Saint-Quentin-en-Yvelines / Paris-Saclay.*

## Ambitious research programs at Institut Curie

Defined as a research priority in France by the "Cancer Plan 2021-2030", triple-negative breast cancer is the focus of much work at Institut Curie. Researchers are advancing on all fronts, to better understand this pathology, identify therapeutic targets, propose biomarkers predictive of response to treatment and combat metastases.

The Institut Curie has launched a fundamental and clinical research program called [CASSIO-PEIA](#), led by Dr. Fatima Mechta-Grigoriou<sup>2</sup> and Prof. François-Clément Bidard. This Hospital-University Health Research (RHU) program is co-financed by the French National Research Agency, Institut Curie and industrial partners. The project aims to gain a better understanding of triple-negative breast cancers, and in particular their heterogeneity, in order to identify at diagnosis those patients who could develop resistance to treatment. The teams will evaluate **new methods for detecting metastases and early recurrence**. The ambition is to **develop novel therapies** targeting fibroblasts, a very abundant cell type in tumors, not yet targeted therapeutically. This innovative program is already behind the Skyline and Cupcake trials.

Dr Céline Vallot<sup>3</sup> is dedicated to **personalizing treatments** by scrutinizing the epigenetic identity cards of tumor cells. Using the "Single Cell" method, she identifies at an early stage the profiles responsible for the **transformation of healthy cells into cancer cells**. These discoveries could support the development of new diagnostic tools and the identification of innovative therapeutic targets.

Dr Philippe Chavrier<sup>4</sup>'s project focuses on the **components of the environment in which metastatic cells develop**, revealing the biological parameters that define an unfavorable prognosis. His recent work has highlighted the novel role of a signaling pathway, offering promising prospects for new therapeutic possibilities. He was also awarded the [Grand Prix Ruban Rose 2022](#) for his innovative project on the development of invasive tumor cell behavior in breast cancer.

The work of Dr Albertas Navickas<sup>5</sup>, winner of the [2023 Rose Avenir ribbon](#) award, helps to explain **the mechanisms that lead breast cancer cells to migrate and develop lung metastases**.

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<sup>2</sup> Outstanding Research Director at Inserm, Head of the Stress and Cancer team at the Cancer, Heterogeneity, Instability and Plasticity (CHIP) unit - U830 Inserm

<sup>3</sup> Directrice de recherche au CNRS, cheffe de l'équipe Dynamique de la plasticité épigénétique dans le cancer au sein de l'unité Dynamique de l'information génétique : bases fondamentales et cancer (UMR3244 / CNRS / Sorbonne Université) et du département de recherche translationnelle

<sup>4</sup> CNRS Research Director, head of the Membrane and Cytoskeleton Dynamics research team at the Cell Biology and Cancer unit (UMR144 / CNRS / Sorbonne University).

<sup>5</sup> Inserm Research Fellow, RNA, tumor microenvironment and metastasis team within the Genome Integrity, RNA and Cancer Unit (CNRS UMR3348 / Université Paris-Saclay)

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### About Institut Curie

Institut Curie, France's leading cancer center, combines an internationally renowned research center with a cutting-edge hospital group, treating all types of cancer, including the rarest. Founded in 1909 by Marie Curie, Institut Curie has 3 sites (Paris, Saint-Cloud and Orsay) with over 3,700 researchers, physicians and health professionals working on its 3 missions: treatment, research and teaching. A foundation with public utility status, Institut Curie is authorized to accept donations and bequests, and thanks to the support of its donors, is able to accelerate discoveries and improve patient treatment and quality of life. Pour en savoir plus : [curie.fr](http://curie.fr), [Twitter](#), [Facebook](#), [LinkedIn](#), [Instagram](#)