GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

PRESS RELEASE

Villejuif, 23 April 2026

A NOVEL TRIPLE THERAPY SHOWS PROMISING SIGNS OF EFFICACY IN LOCALISED LUNG CANCER

The MATISSE study, presented by Professor Fabrice Barlesi, CEO of Gustave Roussy, during a plenary session on clinical trials at the AACR congress, evaluated the addition of a new molecule to the therapeutically validated combination already used for certain patients with non-small cell lung cancer. This novel triple therapy has demonstrated initial promising clinical effects.

Non-small cell lung cancers account for 85 to 90% of the more than 52,000 new cases of lung cancer diagnosed each year in France[1]. This condition remains the 3rd most common cancer in women and the 2nd in men, as well as the leading cause of cancer-related death in men. Identifying new treatment options remains a major public health challenge.

The arrival of immunotherapy over the past decade has transformed the prognosis of this disease. Designed to stimulate the immune system so that it attacks cancer cells more effectively, this approach produces very long-lasting responses, even in metastatic disease.

A standard based on immunotherapy and chemotherapy

In patients with non-small cell lung cancer diagnosed at an early, operable stage, the combination of immunotherapy and chemotherapy is now the established clinical standard alongside surgery. Both treatments are administered together before the procedure to reduce tumour size, after which immunotherapy alone is continued following the operation to consolidate the therapeutic response and reduce the risk of recurrence. This so-called perioperative regimen surrounds the surgical procedure on both sides.

This approach is associated with a significant rate of complete pathological response — that is, the total absence of living cancer cells detected in the tumour following surgical removal. This is a closely monitored criterion in oncology, as it is associated with a better long-term prognosis. The AEGEAN[2] Phase III clinical trial involving over 800 randomised patients was published in 2023 and reported that 17.2% of patients achieved a complete pathological response with the

[1] https://www.cancer.fr/personnes-malades/les-cancers/poumon/comprendre-la-maladie/l-essentiel
[2] Heymach, J. V., et al. (2023). *Perioperative durvalumab for resectable non–small-cell lung cancer*. *New England Journal of Medicine*, 389(18), 1672–1684. https://doi.org/10.1056/NEJMoa2304875

immunotherapy/chemotherapy combination, compared with 4.3% with chemotherapy alone, among patients with operable non-small cell lung cancer.

Addition of an innovative molecule

Nevertheless, a significant proportion of patients show resistance to immunotherapy, which limits its effectiveness. To address this issue, the MATISSE phase II single-arm study, sponsored by Innate Pharma, evaluated the benefit of adding a new molecule to the immunotherapy/chemotherapy combination. IPH5201, co-developed by Innate Pharma and AstraZeneca, is a monoclonal antibody that targets the CD39 enzyme. This enzyme is expressed by cells in the tumour microenvironment in several cancer types, including non-small cell lung cancer.

CD39 plays an essential role in balancing the immune system and preventing it from going into overdrive, but it can also be co-opted by tumours to evade immune detection. It has a notably "immunosuppressive" role — that is, it modifies the tumour environment by reducing inflammation. By neutralising CD39 enzyme activity, IPH5201 aims to reactivate the tumour's inflammatory environment in order to enhance the effects of immunotherapy treatments.

In a previous phase I clinical trial, IPH5201 administered alone or in combination with durvalumab (anti-PD-L1) was well tolerated. The MATISSE trial enrolled 40 patients with early-stage, operable non-small cell lung cancer. They received a triple therapy comprising chemotherapy, immunotherapy (durvalumab), and IPH5201 before surgery. Immunotherapy and IPH5201 were continued following the operation.

Initial promising clinical results

The primary objective of the MATISSE study was to assess the safety and efficacy of this triple therapy. The results show that it presents a favourable safety profile, with no new adverse effects compared with the reference therapeutic combination. Overall, the mean complete pathological response rate was 27.5%.

A more detailed analysis of the results reveals that patients whose tumour expresses the PD-L1 protein — a biomarker for immunotherapy — show higher response rates to this triple therapy. 35.7% of PD-L1-positive patients with a marker expression level of 1% or above (n=28) achieved a complete pathological response. Where PD-L1 expression was 50% or above (n=14), one in two patients responded.

Beyond these clinical results, the MATISSE study also enabled the exploration of biomarkers that may better predict response to the triple therapy. Analyses conducted during the trial show that IPH5201 induces complete and sustained saturation of the CD39 enzyme in patients' blood, confirming that the drug is acting on its intended target. A promising trend was also observed: patients who achieved treatment responses had, at baseline, higher densities of CD39+ cells and CD8+ lymphocytes in their tumour. These immune cells could therefore serve as an early signal for identifying patients most likely to benefit from this new therapeutic approach.

"*The results of the MATISSE study are encouraging. They suggest there could be value in adding IPH5201 to the current therapeutic standard for early-stage, operable non-small cell lung cancers. This triple therapy showed promising rates of complete pathological response among patients at the time of surgery. In a small sub-population of patients whose tumours strongly express the PD-L1 marker, this rate even reaches 50%. These initial data must now be confirmed in a larger number of patients through randomised comparative clinical trials*," concludes Professor Fabrice Barlesi.

Source

Abstract available online on the AACR website:
https://www.abstractsonline.com/pp8/#!/21436/presentation/11994

About Gustave Roussy

Ranked first in France, first in Europe and sixth in the world, Gustave Roussy is a centre of global expertise entirely dedicated to patients living with cancer. The Institute is a founding pillar of the Paris-Saclay Cancer Cluster. Source of therapeutic innovations and diagnostic breakthroughs, the Institute welcomes more than 54,000 patients each year, including 2,760 children and adolescents, and develops an integrated approach combining research, care and teaching. An expert in rare cancers and complex tumours, Gustave Roussy treats all cancers at all stages of life. It offers its patients personalised care that combines innovation and humanity, taking into account both care and the physical, psychological and social quality of life. With 4,000 employees at two sites, Villejuif and Chevilly-Larue, Gustave Roussy brings together the expertise essential for high-level cancer research; 40.5% of treated patients are included in clinical studies. To find out more about Gustave Roussy and follow the Institute's news: www.gustaveroussy.fr/en , X, Facebook, LinkedIn, Instagram et Bluesky.

PRESS CONTACTS

GUSTAVE ROUSSY :
Claire Parisel and Léona Pinto – presse@gustaveroussy.fr - Tél. +33 1 42 11 50 59 – +33 1 42 11 63 59 – +33 6 17 66 00 26