PRESS RELEASE

ESMO 2024 – *Proffered Paper Session*

Villejuif, 13 September 2024

A NEW MEDICALLY PROMISING ANTIBODY CONJUGATE FOR METASTATIC BREAST CANCER

Dr. Barbara Pistilli, Head of Gustave Roussy's Breast Pathology Committee, presents the encouraging results of a phase II therapeutic trial, ICARUS-BREAST01, to the ESMO congress. It focuses on a new drug-antibody conjugate against metastatic breast cancer. Antibody drug conjugates combine an antibody targeting the tumour cell with chemotherapy to deliver treatment directly to the tumour.

Abstract no. 340O presented orally by Dr Barbara Pistilli on Friday 13 September at 4.10pm.

Watch the video online.

Despite advances in screening and treatment, breast cancer remains the most common cancer among women, with 2.3 million new cases and more than 600,000 deaths in 2020 (1). In recent years, CDK4/6 inhibitors combined with hormone therapy have revolutionised the management of patients with hormone-dependent metastatic breast cancer, significantly improving their survival. However, the tumour most often ends up becoming resistant to these drugs. Few effective therapeutic agents are then available for additional treatment.

Patritumab deruxtecan (HER3-DXd) is a drug-antibody conjugate that binds an anti-HER3 antibody to chemotherapy (topoisomerase-I inhibitor). It has already been evaluated in a phase I trial and a phase II study in patients with different types of metastatic breast cancer. ICARUS-BREAST01, sponsored by Gustave Roussy, is a French academic single-arm, phase II, multi-centre study evaluating the activity, safety, and biomarkers of response and resistance to this drug-antibody conjugate in patients with hormone receptor-expressing and HER2 receptor-negative metastatic breast cancer.

ICARUS-BREAST01 evaluates 99 adult patients who received patritumab deruxtecan every 3 weeks until disease progression or unacceptable toxicity. All patients included had a tumour that had become resistant to CDK4/6 inhibitors and one line of chemotherapy.

Identifying resistance factors

The results show that as of 16 April 2024, 19 of the 99 patients in the study were still on treatment. With a median follow-up of 15.3 months, the response rate was 53.5%, with a median duration of response of 8.7 months and median progression-free survival of 9.4 months. The most common adverse events were fatigue, nausea and diarrhoea. *"With conventional treatments used as a third-line chemotherapy, the response rate is lower and progression-free survival is in the region of 4 to 6 months*, says Dr Pistilli, *so these results are very encouraging. »*

Moreover, as part of this work in exploratory analyses, the researchers also identified the factors governing the response to this treatment. Thus, it was demonstrated that the level of HER3 receptors in the tumour was not a factor influencing the response and were able to observe that this response may be dependent on the distribution of HER3-positive cells within the tumour and on the better intra-tumoral distribution of the drug.

Finally, the researchers also demonstrated that activating a drug-induced immune response against the tumour could lead to a better response. *"This drug-antibody conjugate, patritumab deruxtecan, therefore appears to be a promising potential new therapy in advanced forms of hormone-dependent breast cancer, although further studies are needed to confirm these data,*" concludes Dr Pistilli.

This work, carried out in partnership with Daiichi Sankyo and MSD, is part of the Unlock medical scientific programme, developed by Gustave Roussy, which aims to understand and circumvent the mechanisms of resistance developed by patients' bodies to innovative therapies.

(1)Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA: A Cancer Journal for Clinicians 2024;74(1):12–49.

***Abstract* no. 340O**

Efficacy, safety and biomarker analysis of ICARUS-BREAST01: A phase II study of patritumab deruxtecan (HER3-DXd) in patients (pts) with HR+/HER2- advanced breast cancer (ABC)

Friday 13 September 2024 | 4:10 pm.

About Gustave Roussy

Ranked first in France, first in Europe and fourth 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 nearly 50,000 patients each year, including 3,500 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 4,100 employees at two sites, Villejuif and Chevilly-Larue, Gustave Roussy brings together the expertise essential for high-level cancer research; 40% of treated patients are included in clinical studies. To find out more about Gustave Roussy and follow the Institute's news: https://www.gustaveroussy.fr/en, X, Facebook, LinkedIn, Instagram.

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