PRESS RELEASE

ASCO 2024 - *Oral session*

Villejuif, 31 May 2024

PROMISING RESULTS WITH ANTI-TROP2 DRUG-CONJUGATED ANTIBODY IN METASTATIC LUNG CANCER

Drug-conjugated antibodies are a rapidly developing therapeutic class in oncology. The principle of these drugs is based on binding an anti-tumour drug (chemotherapy molecule) via a binding system (called linker) to an antibody specifically directed against a target expressed on the surface of tumour cells. The aim is for this chemotherapy molecule to be delivered directly to cancer cells, theoretically without affecting healthy cells. Many studies are ongoing with this new therapeutic class.

Abstract n°8501 presented orally by Prof. Planchard on Friday 31 May at 2:57 p.m. UTC-5

This oral presentation is one of the 135 presentations on the agenda for this 2024 edition of ASCO, in which Gustave Roussy's research physicians took part, including 29 oral presentations. Gustave Roussy is present in many fields of expertise, attesting to the quality of the research carried out there and its international recognition.

A trial coordinated by Gustave Roussy, ICARUS-Lung01, presented to ASCO on 31 May 2024 by Prof. David Planchard, Head of the Thoracic Pathology Committee, showed that for patients with non-small cell, metastatic and therapeutically failed lung cancers, these drug-conjugated antibodies enable a significant response rate and improve progression-free survival. These encouraging interim results provide new hopes against metastatic lung cancer.

This trial was conducted by Gustave Roussy as part of the UNLOCK medical-scientific programme, which aims to understand the mechanisms of action of and resistance to innovative treatments.

ICARUS-Lung01 is a French phase II, single-arm, multicentre trial conducted at eight centres and led by Prof. David Planchard and Dr. Barbara Pistilli, Head of the Breast Pathology Committee. Its objectives were to evaluate the clinical benefit of a drug-conjugated anti-TROP2 antibody in patients with advanced lung cancer, identify its tolerance profile, and biomarkers of response or resistance to treatment.

A total of 100 patients with metastatic cancer and in therapeutic deadlock after one to three lines of treatment (chemotherapy and/or immunotherapy or targeted therapy) were included in this trial in 2022. The drug-conjugated antibody used in this context was an anti-TROP 2 antibody targeting a protein overexpressed on the surface of the tumour cell in 80% of lung cancers. This antibody is bound to a chemotherapy molecule, a topoisomerase-1 inhibitor, via

a “linker”, in this case a peptide bond that will cleave when the antibody enters the tumour cell to release the chemotherapy molecule. This is a complex treatment whose mechanisms of action remain poorly understood. The effect of the chemotherapy drug on tumour cells and on the peri-tumour environment is certain, and that of the antibody and linker is likely, particularly on the peri-tumour immune system. Not all antibodies will reach their cellular target and a certain amount of the drug is released into the peri-tumour environment and general circulation.

Patients in this trial had either squamous cell lung cancer (18%) or nonsquamous cell lung cancer (82%). All patients received an infusion of drug-conjugated antibodies every three weeks, as long as disease did not progress or potential toxicity did not require discontinuation of treatment. Additionally, a “fresh” biopsy of a tumour lesion was collected from all patients prior to initiation of treatment, during treatment, and during tumour progression to assess biomarkers associated with response or resistance to treatment.

The results show a promising response rate of approximately 26%. In total, a quarter of patients had at least 30% lesion reduction. “For responder patients, the median duration of response is 7 months,” said Prof. David Planchard, “these results are all the more important as the patients included in this trial were in therapeutic deadlock and had already received standard treatments for this disease”.

Above all, the trial identified a number of factors associated with a good therapeutic response. The analysis showed in particular that the clinical benefit is mainly found for non-squamous cell tumours (response rate of 30.5%) compared to squamous cell tumours (response rate of 5.6%). Similarly, median progression-free survival was 4.8 months for non-squamous cell tumours and 2.9 months for squamous cell tumours. Additionally,12 patients had a tumour with a genetic mutation accessible to targeted therapy (11 patients with the EGFR mutation and one patient with the BRAF mutation). For patients with the EGFR mutation, the therapeutic benefit appeared promising, with a 50% response rate and a median progression-free survival of 6.8 months. Non-squamous cell tumours and those with an EGFR+ activating mutation (while remaining cautious due to the small number of patients) appear as two strong criteria for predicting response to this anti-TROP2 drug-conjugated antibody.

In terms of side effects, the main toxicities (primarily grade 1–2) were mucitis (inflammation of the mouth in approximately 48% of patients), nausea (47% of patients) and fatigue (33%). At the last data analysis in April 2024, six patients were still included in the study.

Preliminary analyses with other biomarkers are underway. In particular, they show that patients with low expression of the TROP2 protein on the surface of tumour cells appear to have a poorer response to these drug-conjugated antibodies. However, these data must be confirmed in order to best select patients who could benefit from this innovative therapy.

"Our *results are very encouraging for patients with advanced non-squamous lung cancer and those with molecular alteration such as the EGFR mutation," said Prof. Planchard,* "They *pave the way for a new line of treatment for some patients with metastatic lung cancer".*

Abstract no. 8501 - *ICARUS-LUNG01: A phase 2 study of datopotomab deruxtecan (Dato-DXd) in patients with previously treated advanced non-small cell lung cancer (NSCLC), with sequential tissue biopsies and biomarker analysis to predict treatment outcome* – Oral session – Friday 31 May 2024 | 4:42 p.m. UTC-5.

Background on Gustave Roussy

Ranked as the leading French and European Cancer Centre and fourth in the world, Gustave Roussy is a centre with comprehensive expertise and is devoted entirely to patients suffering with cancer. The

Institute is a founding member of the Paris Saclay Cancer Cluster. It is a source of diagnostic and therapeutic advances. It caters for almost 50,000 patients per year and its approach is one that integrates research, patient care and teaching. It is specialized in the treatment of rare cancers and complex tumors and it treats all cancers in patients of any age. Its care is personalized and combines the most advanced medical methods with an appreciation of the patient's human requirements. In addition to the quality of treatment offered, the physical, psychological and social aspects of the patient's life are respected. 4,100 professionals work on its two campuses: Villejuif and Chevilly-Larue. Gustave Roussy brings together the skills, which are essential for the highest quality research in oncology: 40% of patients treated are included in clinical studies.

For further information**: www.gustaveroussy.fr/en, X, Facebook, LinkedIn, Instagram**

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