GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

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Press release

LUNG CANCERS:
hopes for conjugated antibodies

Some non-small cell cancers of lung that are resistant to therapy might benefit from a novel treatment combining an antibody with a cytotoxic drug. The results of an early trial conducted at Gustave Roussy, presented in an oral session at ASCO 2020, show that an agent consisting of an antibody complexed with a maytansine derivative has anti-tumour activity without major adverse effects in patients whose tumour overexpresses CEACAM5.

One of the recent ambitions in oncology has been to develop medication in which antibodies capable of identifying cancer cells are complexed with a cytotoxic agent, thus enabling direct targeting of the tumour cell. These conjugated antibodies or antibody drug conjugates (ADC) would seem at the outset to possess two qualities: the ability to destroy cancer cells by virtue of delivering higher cytotoxic concentrations than is possible with conventional chemotherapy while at the same time sparing healthy cells. This principle has already been used in the treatment of metastatic breast cancers over-expressing HER2 and validated in that of Hodgkin's lymphomas. It might also provide a novel therapeutic pathway in treatment of certain lung cancers according to findings in the phase I/II study presented in an oral session at the ASCO Conference by Dr. Anas Gazzah, oncologist in the Drug Development Department (DITEP) at Gustave Roussy. These promising results do show that such medication could control the disease without having major side effects in 64% of locally advanced or metastatic non-small cell, non-squamous cell lung cancers that were strongly overexpressing CEACAM5 and displaying resistance to other treatment. The mean duration of response was 5.6 months.

The conjugated antibody, whose safety and efficacy in man has been evaluated for the first time by the research team in patients with advanced solid tumours, goes for the present by the code name SAR408701. It comprises a monoclonal anti-CEACAM5 antibody and a cytotoxic maytansine derivative, DM4, an anti-tubulin agent which induces cell death. The antibody detects and targets cells expressing the carcinoembryonic antigen CEACAM 5. This protein has a role in the mechanism of cell adhesion and is present in the body during fetal development. Its expression in adults is very limited but it is found in a number of tumours including those of the gastrointestinal tract and adenocarcinoma of lung.

Oral presentation
by **Dr. Anas Gazzah**

READ THE ABSTRACT
N° 9505

EXPLANATIONS IN VIDEO

Anti-tumour efficacy of conjugated antibody in patients in treatment failure who have non-small cell lung cancers (the majority of lung cancers).

The data presented at ASCO specifically concern the action of this conjugated antibody on locally advanced or metastatic non-squamous cell, non-small cell lung cancer (NSCLC). These constitute the majority of lung cancers and are most commonly treated, other than surgically, with one or more lines of chemotherapy (platinum salts combined with pemetrexed and taxanes), sometimes concomitantly with or followed by anti-PD(L)1 immunotherapy. ***"Pre-screening of tumour specimens has shown that 44% of these tumours express carcinoembryonic antigen strongly or moderately (20 and 24% respectively),"*** **explained Dr. Gazzah.**

This overexpression was the principal inclusion criterion for the study. Patients with NSCLC were assigned to one of two cohorts depending on whether they expressed CEACAM5 strongly in more than 50% of tumour cells (64 patients) or moderately (28 patients). The 92 patients were recruited from several centres in France, Spain and Korea. All of them had received at least three lines of treatment prior to receiving conjugated anti-CEACAM5 antibody by intravenous injection (100 mg/m^2) at two-weekly intervals. Tumour response was assessed by CT scan every eight weeks.

The final analysis of the data at 9th March 2020 showed that only a third of all the recruited patients had not responded to treatment. The level for control of disease was above 60% in both groups. The level of tumour response, principal end-point of the study, was higher in those patients strongly overexpressing CEACAM5 compared with those in the "moderate" group (20.3% vs 7.1%). The median duration of the response was estimated at 5.6 months, but this period was sometimes prolonged in "overexpressing" patients: ***"some have been on treatment for more than two years"*** **pointed out Dr. Gazzah.** Ocular side effects were predominant in the unwanted effects noted. These arose after the early injections during the first 4 cycles. ***"The ocular events are common side effect of ADCs using antitubulin agents,"*** **explained Dr. Gazzah,** ***"but they are reversible and can be managed by a reduction in dose or postponement of the injection and do not appear to represent a limiting factor."***

A phase III trial is due to commence. Its objective is to compare the benefit of conjugated anti-CEACAM5 antibody with single agent chemotherapy using docetaxel, in patients with treatment failure after receiving one standard first line therapy (chemotherapy + anti PD1/PD-L1).

Only a third of the patients did not respond to treatment.

A phase III trial to evaluate this conjugated antibody has commenced.

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Regarding Gustave Roussy
Gustave Roussy, the leading cancer center in Europe, is a comprehensive hub of expertise in oncology, entirely devoted to patients. It employs 3,100 professional staff engaged in patient care, research and teaching.

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