EARLY CLINICAL TRIALS
FIRST EVALUATIONS OF THE THERAPIES OF THE FUTURE

Early trials at Gustave Roussy are led by the Drug Development Department (DITEP), which is directed by Professor Jean-Charles Soria. Four of the DITEP doctors presented promising results on Saturday, 30th May and Monday, 1st June.

Dr Andrea Varga showed that an immunological therapeutic agent shown to be effective in melanoma produced good results in patients with advanced ovarian cancer which had not responded to more than one drug. Dr Eric Angevin assessed a new immunological agent (anti-CD26) for the first time in man. Dr Antoine Hollebecque studied a combination of two known anti-cancer agents analysing their activity in patients with solid tumours where previous medication had been ineffective. Dr Anas Gazzah reported results obtained in solid tumours using a different combination of two targeted drugs.

NEW HOPE FOR IMMUNOTHERAPY THERAPY IN OVARIAN CANCER

Pembrolizumab is a highly-selective monoclonal antibody which relieves inhibition of T lymphocyte anti-cancer activity by blocking the interaction between PD-1 and its ligands (PD-L1, L2). It was recently evaluated in melanoma where it has very convincingly been shown to be superior to another immunological agent (phase III study).

The PD-L1 ligand may be over-expressed in ovarian tumours and this phenomenon may contribute to their invasiveness.

The KEYNOTE-028 phase Ib study was delivered as an oral communication on Monday, 1st June by Dr Andrea Varga, a doctor in the DITEP team. This study assessed the efficacy and safety profile of pembrolizumab in 26 patients with advanced ovarian cancer: Interim results from a phase Ib study.

Andrea Varga, Sarina Anne Piha-Paul, Patrick Alexander Ott, Janice M. Mehnert, Dominique Berton-Rigaud, Elizabeth A. Johnson, Jonathan D. Cheng, Sammy Yuan, Eric H. Rubin, Daniela E. Matei
ovarian cancer, cancer of the Fallopian tubes or primary peritoneal cancer. The PD-L1 ligand was over-expressed in these tumours. The patients had experienced at least one therapeutic failure. Pembrolizumab was administered at a once-weekly dose of 10 mg/kg for two years or until tumour progression was noted or side effects became too prominent. The commonest adverse effects were: fatigue (42.3%), anaemia (30.8%) and loss of appetite (30.8%). A reduction in tumour size was observed in 23% of the patients in whom the previous chemotherapeutic load had been substantial (failure of 2 to 4 lines of treatment). At present 6 patients remain on pembrolizumab in the context of this trial.

**FIRST STUDY IN MAN OF A NEW ANTIBODY DIRECTED AGAINST CD26**

CD26 is a biomarker which is strongly expressed on the cell surface of certain cancers such as mesothelioma. It is also involved in immune regulation. YS110 is a new antibody directed against CD26 and its potential has been demonstrated in pre-clinical studies. Dr Eric Angevin led a study to evaluate its effects in man for the first time. This involved 34 patients with solid tumours expressing CD26, principally advanced mesothelioma, so as to determine a recommended dose and to assess its safety profile. YS110 was administered at a dose ranging from 0.1 to 6 mg/kg without reaching dose-limiting toxicity. The adverse effects seen were: asthenia (33.3%), hypersensitivity (30%), shivering (13.3%), pyrexia (13.3%), nausea (13.3%), vomiting (10%) and headache (10%). These were not dose-dependent. The initial results, presented on Saturday, May 30th, showed that disease was stabilised in 13 of the patients treated (of the 25 whose results could be assessed) and that YS110 appears to be well tolerated.

**EVALUATION OF THE SYNERGISTIC EFFECT OF TWO KNOWN THERAPEUTIC AGENTS**

Temsirolimus is a selective inhibitor of the mTOR protein, which is currently used to treat renal carcinoma and mantle-cell lymphoma. Cetuximab is a monoclonal anti-EGFR antibody and is used in metastatic colorectal cancer and in locally advanced squamous cell carcinoma of the head and neck. Their synergistic effects had been evaluated in pre-clinical studies. In a Gustave Roussy-sponsored phase I study, Dr Antoine Hollebecque examined the activity and safety of a combination of these two drugs in 39 patients with a variety of solid tumours, who had already received more than one treatment. The objectives were to ascertain the recommended dose, to study the pharmacokinetics and to examine the safety profile of the drug combination. The recommended dose was fixed at 250 mg/m²/week for cetuximab and 25 mg/week for temsirolimus. The results presented on 30th May demonstrate that this combination has a role, particularly in those patients who have molecular

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**Flash and find #2519**

2. First-in-human phase I administration of YS110, a monoclonal antibody directed against the CD26 immunostimulatory molecule in advanced cancer patients.

**Flash and find #2599**


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abnormalities affecting the EGFR and/or the PI3K pathways. The safety profile is acceptable.

**COMBINATION OF TWO TARGETED THERAPEUTIC AGENTS**

In another phase I study, presented on Saturday, 30th May, Dr Anas Gazzah reported efficacy data from a study in 49 patients of the two targeted drugs, cetuximab and afatinib, in combination. This combination was tolerated and the recommended doses were 40 mg daily for afatinib and 250 mg/m² weekly for cetuximab. Prolonged disease stability was observed both in cancers of the upper airways and squamous cell cancer of lung.
The Gustave-Roussy medical researchers reveal their research findings in 56 presentations at the American Society of Clinical Oncology Conference. The ASCO scientific committee selected 22 oral communications, 5 of which were to be presented directly by the Institute, 7 posters for discussion, 5 of which to be presented by Gustave-Roussy, and 25 posters.

At this 51st meeting of the most important world conference in oncology, Gustave Roussy confirms its leading position in two therapeutic fields which are being absorbed into day-to-day management and are resulting in changes in practice within the Department of Medical Oncology (DMO): immunotherapy which is being developed in new disease areas, and targeted therapies and novel approaches to tumour resistance to treatment. This 2015 meeting will also be noteworthy for the early evaluation through phase I clinical trials of what will become tomorrow’s therapies, in particular within DITEP (Drug Development Department) at Gustave Roussy.