GUSTAVE ROUSSY AT THE ASCO

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29th MAY

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2015

PRESENTATIONS
OF GUSTAVE ROUSSY
AT THE ASCO 2015

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

2015 ASCO Annual Meeting
Illumination&Innovation
transforming data into learning
May 29-June 2, 2015
McCormick Place | Chicago, Illinois
ASCO

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GUSTAVE ROUSSY AT THE ASCO

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ASCO 2015 :
ASCO PRESENTATIONS WHICH CONFIRM THE LEADERSHIP OF GUSTAVE ROUSSY IN THE FIELD OF TARGETED THERAPIES AND THE IMMUNOTHERAPY

ASCO
MAY 29TH – JUNE 2ND, 2015

51 TH CONGRESS
American Society of Clinical Oncology (Asco, Chicago, USA, May 29th – June 2nd 2015).

ABOUT GUSTAVE ROUSSY
Gustave Roussy, the first comprehensive cancer centre in Europe, is a global centre of expertise in the fight against cancer wholly dedicated to patients. It brings together on a same site 3,000 professionals whose missions are the care, research and education.
– www.gustaveroussy.fr

Gustave Roussy's medical researchers will unveil their research work through 56 presentations at the congress of the American Society of Clinical Oncology. The scientific committee of ASCO has selected 22 oral communications including 5 directly submitted by the Institute, 7 posters/discussions including 5 submitted by Gustave Roussy and 25 posters.

For this 51th edition of the most important world congress of cancer, Gustave Roussy confirmed its leadership in two therapeutic strategies which become daily supports and induce a change of the practices within the Oncological Medicine Department (OMD): the immunotherapy which develops in new pathologies as well as the targeted therapy and new approaches against the resistance that tumours may develop. This 2015 edition will be also marked by the early assessment of tomorrow's therapies during phase I clinical trials, notably within the DITEP (Drug Development Department) of Gustave Roussy.

Find all the news of Gustave Roussy at the Asco 2015 starting from May 29th
www.gustaveroussy.fr/asco2015


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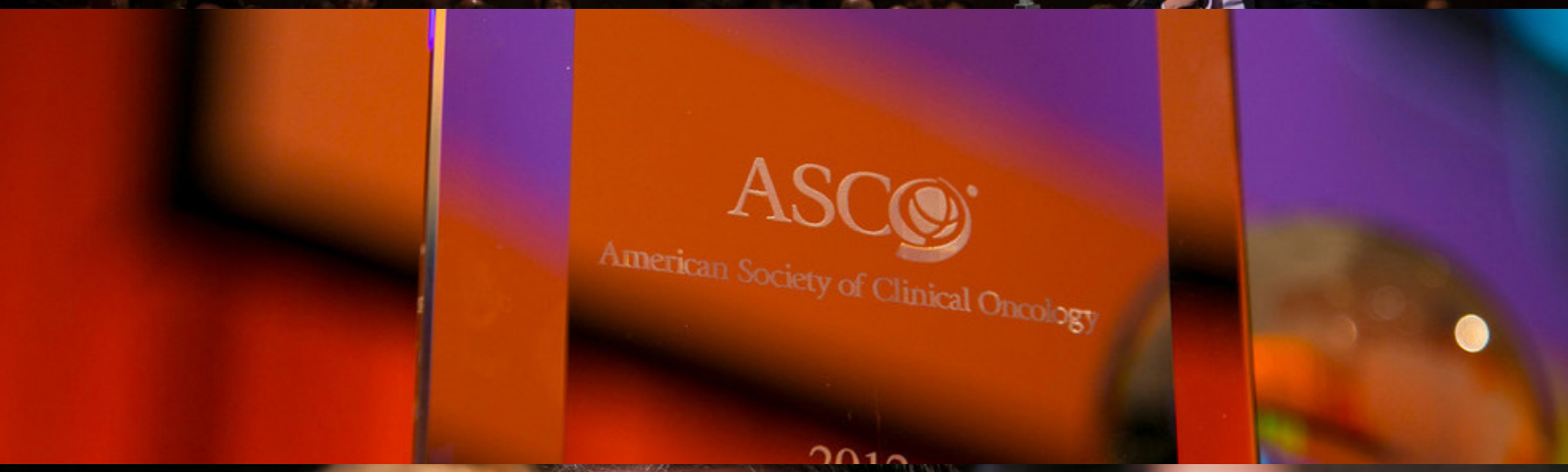
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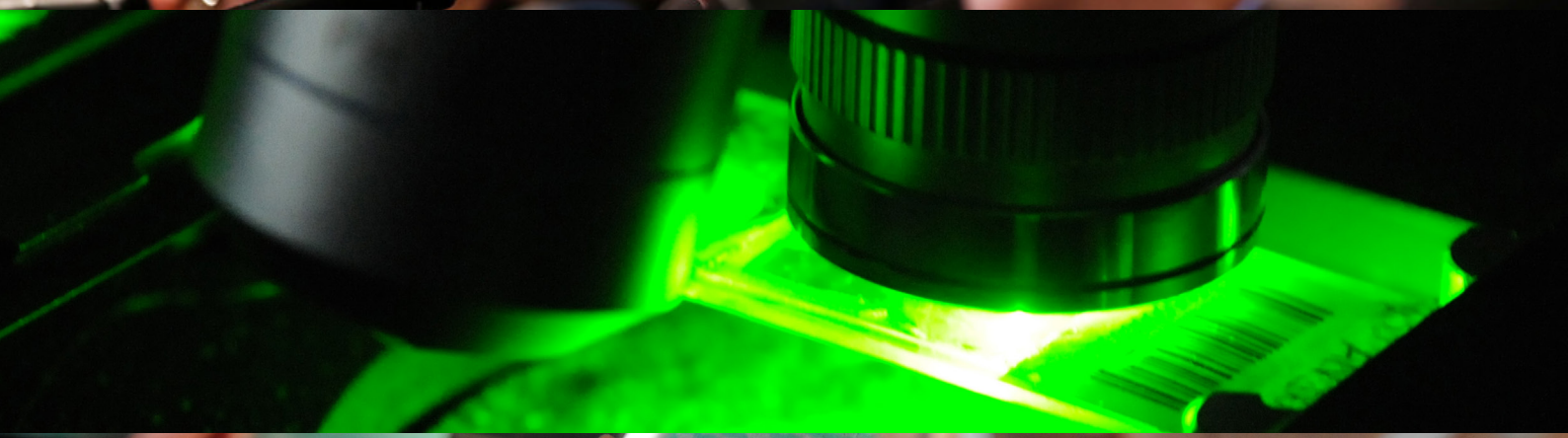

1
EARLY PHASE AND NEW DRUGS

An early clinical test (or phase I trial) is to assess the security of employment of a new molecule (administered alone or in combination with another therapy), its future in the body, the side effects that it can provoke in Man and to assess its antitumour activity.

The early tests are conducted at Gustave Roussy by the Drug Development Department(DITEP) headed by Prof. Jean-Charles Soria.

NEW HOPE IN IMMUNOTHERAPY FOR OVARIAN CANCER

It was previously observed that the ligand PD-L1 is overexpressed in the ovary cancer.
The pembrolizumab is a monoclonal antibody highly selective which blocked the interaction between PD-1 receptor present on the surface of T lymphocytes and its ligands (PD-L1, L2). During an oral presentation, Dr. Andrea Varga, oncologist at DITEP, will expose the intermediate results of a phase Ib study of pembrolizumab (antibodies anti-PD-1) in patients with advanced cancer of the ovary expressing PD-L1. The tumour reductions are observed in 23% of the heavily pre-treated Patients with chemotherapy (2 to 4 lines)

Oral Presentation (Abstract 5510), on Monday, June 1st, at 15h12 (Chicago time), room E354b
Summary available on http://abstracts.asco.org/156/AbstView_156_147724.html
Antitumor activity and safety of pembrolizumab in patients (pts) with PD-L1 positive advanced ovarian cancer: Interim results from a phase Ib study.

FIRST STUDY OF A NEW ANTIBODY DIRECTED TOWARD THE CD26 IN HUMANS

The CD26 is a biomarker strongly expressed at the cell surface of certain cancers such as mesothelioma.
Dr. Eric Angevin, doctor at the DITEP, will present the results of a first encouraging evaluation conducted among 34 patients with solid tumours, mainly of advanced mesothelioma, the YS110, a new antibodies directed against the biomarker CD26, a molecule of immunostimulation.

Poster, Saturday, May 30th at 8h00 (Chicago time), room S Hall A, followed by a discussion on the same day at 13h15 room S406.

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 # 5510

Summary available on http://abstracts.asco.org/156/AbstView_156_146929.html
First-in-human phase I administration of YS110, a monoclonal antibody directed against the CD26 immunostimulatory molecule in advanced cancer patients.

ASSESS THE SYNERGISTIC EFFECT OF TWO THERAPIES

In a phase I clinical study promoted by Gustave Roussy, Dr. Antoine Hollebecque, Doctor at the DITEP, was studied on 39 patients with various types of solid tumours, the effect and toxicity of 2 treatments combined, the temsirolimus (a selective inhibitor of the protein mTOR) and cetuximab (a monoclonal antibody anti-EGFR) whose synergistic effect had been evaluated at preclinical studies. The objective was to determine the dose of recommended use, the pharmacokinetics and the safety profile of the combination of these 2 therapies.

Poster, Saturday, May 30th at 8h00 (Chicago time), room S Hall A
Summary available on http://abstracts.asco.org/156/AbstView_156_152775.html
Phase I study of temsirolimus in combination with cetuximab in patients with advanced solid tumors.

ASSOCIATION OF TWO TARGETED THERAPIES

In another phase I research, Dr Anas Gazzah, doctor at the DITEP, reports the data of efficiency of two targeted therapies cetuximab-afatnib. This association has been tested with 49 patients. It is tolerable and the recommended dose has been 40 mg/day of afatinib and 250 mg/m2 of cetuximab on a weekly basis. Extended stabilities have been observed in the cancers of cancers of the upper aerodigestive tract and squamous cell carcinoma of the lung.

Poster ,Saturday 30th May at 08h00 (Chicago time) Room S Hall A
Synopsis available on http://abstracts.asco.org/156/AbstView_156_145922.html
Phase Ib study of afatinib plus standard-dose cetuximab in patients (pts) with advanced solid tumors.

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PROOF OF CONCEPT IN IMMUNOTHERAPY

Immunotherapy is to wake up the immune system against cancer. It is therefore to stimulate by different treatments the immune system in order to enable him to fight the tumour cells. This therapeutic way now benefits from randomised and comparative data that will promote in a short-term the emergence of this therapeutic strategy in daily practice. Gustave Roussy is one of the first comprehensive cancer centre in the world and precursor in immunotherapy.

AFTER THE DEMONSTRATION OF EFFICIENCY, HOW TO BETTER MANAGE THE TOXICITY OF A IMMUNOTHERAY IN THE MELANOMA?

The nivolumab is a monoclonal antibody that is fixed to the PD-1 receiver of T lymphocytes in order to stimulate the immune system and to enable it to effectively combat the tumour. It has demonstrated its effectiveness on the tumour response in many cancers and prolonged the survival of patients with melanoma. However, it may be at the origin of more or less obstructive secondary effects. In this retrospective analysis, including 4 clinical trials from phase I to III at the origin of the recommendations on the use of this molecule in patients with melanoma, Dr. Caroline Robert, dermato-oncologist in the Department of Oncology Medicine and head of the department of Dermatology at Gustave Roussy, identified in these patients the onset of side effects inherent in the nivolumab, including those of immunological order, and proposes a methodology to manage the most important (grade 3-4). This is done notably by adding an immunomodulating agent to the treatment without affecting the tumour response.

Poster, Monday, June 1st at 13h15 (Chicago time), room S hall A, followed by a discussion on the same day at 16h45 (Chicago time) Room S100bc
Summary available on http://abstracts.asco.org/156/AbstView_156_145632.html
Safety profile of nivolumab (NIVO) in patients (pts) with advanced melanoma (MEL): A pooled analysis

Note: Post-Plenary Discussion with Dr. Caroline Robert who will moderate the exchanges that will follow the plenary conference about the melanoma on Saturday, May 31st at 16h00 room S100bc

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DOUBLE IMMUNOTHERAPY IN LUNG CANCER: THE DESIGN OF AN INNOVATIVE STUDY UNVEILED

With approximately 37,000 new Estimated cases in 2010, Lung Cancer is positioned on the 4th rank of Cancers, both genders, but remains however.
The first cause of death by Cancer in France and in the world (source INCa). The bronchial cancers that do not have small cells represent 75 to 80% of all lung cancers.

The multicentre study of phase III, which seeks to include 900 patients in total will be coordinated in France by Dr. David Planchard, pneumo-oncologist in the Department of Oncology Medicine of Gustave Roussy (1st author) and at the global level by the Prof. Jean-Charles Soria, head of the Drug Development Department (DITEP)(last author). The objective is to assess the effectiveness and the safety profile of 2 immunotherapies (MEDI4736 and tremelimumab), alone or in combination, in relation to the treatment of reference, in breast cancer patients with metastatic lung (that does not have small cells) which express PD-L1.

These 2 immunotherapies are acting on 2 different routes of activation of T lymphocytes.
The MEDI4763 is a monoclonal antibody that lifted the inhibition induced by the fixing of the ligand PD-L1 expressed by tumours on the PD-1 and CD 80 receivers of T lymphocytes. As to the tremelimumab, it selectively inhibits the antigen 4 (CTLA4) of cytotoxic T lymphocytes.

The preclinical results and the first tests on man had demonstrated that the simultaneous focus of these 2 ways of activation seems to lead to an additive or synergistic effect in their antitumour activity, with a low toxicity and clinically observable effects at low dose.

Poster, on Monday, June 1st, at 8h00 (Chicago time), room S Hall A
Summary available on http://abstracts.asco.org/156/AbstView_156_147299.html
A phase III study of MEDI4736 (M), an anti-PD-L1 antibody, in monotherapy or in combination with Tremelimumab (T), versus standard of care (SOC) in patients (pts) with advanced Non-Small Cell Lung Cancer (NSCLC) who have received at least two prior systemic treatment regimens (ARCTIC).

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IN OVARIAN CANCERS

Dr. Andrea Varga, oncologist at the DITEP, will expose the intermediate results of a phase Ib study of pembrolizumab (anti-PD-1 antibodies) in patients with advanced ovary cancer expressing PD-L1.

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EARLY PHASE AND NEW MEDICINAL PRODUCTS IN PAEDIATRICS

During the session dedicated to the paediatric oncology, Dr. Birgit Geoerger, onco-paediatrician at Gustave Roussy, will present 2 oral communications regarding phase I trials that evaluates targeted therapy in children.

She will outline the first results of a targeted therapy (ceritinib) which inhibits the KLA pathway in children with different types of tumours that all express KLA mutation. This molecule has already proven its effectiveness in adult patients with non-small cell lung cancer and expressing ALK.

20 Young patients have been included in this international multicentre (22 centres from 10 countries) which has allowed us to determine the recommended dose of ceritinib to use among children and to demonstrate its effectiveness, particularly among the patients with anaplastic lymphoma large cell or a myofibroblastique tumour, whether inflammatory or not.

Oral Presentation, Saturday, May 30th at 16h24 (Chicago time, room S504)
Summary available on http://abstracts.asco.org/156/AbstView_156_146923.html
Phase I study of ceritinib in pediatric patients (Pts) with malignancies harboring a genetic alteration in ALK (ALK+): Safety, pharmacokinetic (PK), and efficacy results.

The other international pediatric test presented by Dr. Birgit Geoerger has focused on the study of dabrafenib (inhibitor of tyrosine kinase of the BRAF way) among 27 children, in relapse or refractory, subject to a tumour bearing a BRAFV600E mutation (glioma of high and low grade, histiocytosis that has Langerhans cells as well as other solid tumours) in order to determine the recommended dose of use for phase II. The dabrafenib is indicated as monotherapy in the treatment of adult patients with unresectable or metastatic melanoma. The results show that a complete response was obtained on the glial tumours. This is the first paediatric study in the world that demonstrates the effectiveness of a targeted therapy on children with a glioma of high grade while no treatment is currently available.

Oral Presentation, Saturday, May 30th at 16h12 (Chicago time, room S504)
Summary available on http://abstracts.asco.org/156/AbstView_156_149751.html
Phase 1 study of dabrafenib in pediatric patients (pts) with relapsed or refractory BRAF V600E high- and low-grade gliomas (HGG, LGG), Langerhans cell histiocytosis (LCH), and other solid tumors (OST).

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THE DEVELOPMENT OF TARGETED THERAPIES IN MANY PATHOLOGIES

Specifically targeting a protein or an action mechanism involved in the development of a tumour to spare the maximum healthy cells is the goal of a targeted therapy. In recent years, the progresses of genomics that are used to determine the genetic characteristics specific to a tumour have participated in the development of targeted therapy. Today this therapeutic strategy in full expansion has not finished demonstrating its potential and Gustave Roussy which is one of the leaders in the development of this approach continues to conduct numerous research studies in this area.

In lung cancer

COMPARE 2 TARGETED THERAPIES

The Prof. Jean-Charles Soria, Leader of the DITEP, will present the results of the Lux-Lung 8 clinical study of phase III in patients with a squamous cell carcinoma of the lung on the progression-free survival of the pathology and the overall survival of 2 targeted therapies, the afatinib compared to the erlotinib, one of the current standards, on the second line of treatment. It is the largest randomised study ever conducted on the second line.
This study shows that the afatinib decreased by 19% the risk of progression of pathology but also the risk of death, compared to the erlotinib.
The response data and quality of life also show the superiority of the afatinib.

Oral Presentation, Sunday, May 31st at 8h24 (Chicago time), room N Hall B1
Summary available on..
http://abstracts.asco.org/156/AbstView_156_145877.html
Afatinib (A) vs erlotinib (E) as second-line therapy of patients (pts) with advanced squamous cell carcinoma (SCC) of the lung following platinum-based chemotherapy: overall survival (OS) analysis from the global phase III trial LUX-Lung 8 (LL8)

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ASSOCIATE TARGETED THERAPIES IN ORDER TO OVERCOME RESISTANCES

In a phase II study conducted in patients with metastatic non-small cell lung cancer which presents a BRAFV600E mutation, Dr. David Planchard, pneumo-oncologist at the Department of Oncology Medicine of Gustave Roussy has combined two targeted therapies which act on 2 different ways, the dabrafenib (inhibitor of the BRAF way) and the trametinib (inhibitor of the MEK way) in order to assess the effectiveness and the toxicity profile of these 2 molecules combined. The dabrafenib only allows you to get an overall ▶▶▶

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response rate of 32 %. Associated with the trametinib, the overall response rate then jumped to 63 %, with manageable secondary effects.

Oral Presentation, Sunday, May 31st at 10h00 (Chicago time), room N Hall B1
Summary available on http://abstracts.asco.org/156/AbstView_156_147124.html
Interim results of a phase II study of the BRAF inhibitor dabrafenib (D) in combination with the MEK inhibitor trametinib (T) in patients (pts) with BRAF V600E mutated metastatic non-small cell lung cancer (NSCLC)

EVIDENCE OF EFFICIENCY OF A 3RD GENERATION EGFR INHIBITOR IN LUNG CANCER

during an oral presentation, the Prof. Jean-Charles Soria, Head of the Drug Development Department (DITEP) of Gustave Roussy will unveil the results of a 3rd generation EGFR inhibitor (rociletinib) obtained in patients with non-small cell lung cancer bearing the T790M EGFR mutation and having previously been treated by one or more inhibitors of EGFR. In the framework of a phase I/II study conducted on 456 patients, the rociletinib has confirmed its effectiveness with an objective response rate of 60% and a control rate of 90 %. The progression free survival is of 10.3 months. In addition, this study demonstrated that the T790M mutation can be detected in the blood and that, in this case, the rate of response remains of 57 %.

Oral Presentation, Sunday, May 31st at 8h12 (Chicago time), room N Hall B1
Summary available on http://abstracts.asco.org/156/AbstView_156_152181.html
Efficacy of rociletinib (CO-1686) in plasma-genotyped T790M-positive non-small cell lung cancer (NSCLC) patients (pts).

IN RARE CANCERS (SARCOMAS)

Dr. Olivier Mir, oncologist in the Department of Oncology Medicine of Gustave Roussy, will present the results of the REGOSARC study, a phase II clinical study, randomised, against placebo in double-blind of a targeted therapy (regorafenib) among 110 patients with leiomyosarcoma or another type of soft tissue sarcoma about the progression free survival and overall survival. The regorafenib is an inhibitor of the tyrosines kinases which has demonstrated its effectiveness on the gastro-intestinal tumours. The results obtained on the sarcomas are promising.

Oral Presentation, Monday, June 1st at 16h12 (Chicago time), room S504
Summary available on http://abstracts.asco.org/156/AbstView_156_144451.html
Activity of regorafenib (RE) in leiomyosarcomas (LMS) and other types of soft-tissue sarcomas (OTS): Results of a double-blind, randomized placebo (PL) controlled phase II trial.

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FEMALE CANCERS

OVARIAN CANCER; WHAT IS THE IMPACT OF A CHEMOTHERAPY ON THE TUMORAL GENOMIC PROFILE AND THE IMMUNE INFILTRATE?

Dr. Alexandra Leary, oncologist in the Department of Oncology Medicine of Gustave Roussy, will present the results of a study on the genetic mutations and the changes made on the immune infiltrate of ovarian tumours following neo-adjuvant chemotherapy. This important information is then used to determine the best treatment (immunotherapy or targeted therapy), to better eradicate residual cancer cells which could lead to relapses.

Note :The Dr Alexandra Leary will present a synopsis of abstracts which identifies the clinical trials of phase II over new molecules evaluated in ovarian cancer resisting a platinum-based chemotherapy Saturday the 30th of May at 17h00 Room E354B

Poster, Saturday, May 30th, at 13h15 (Chicago time), room S hall A
Summary available on http://abstracts.asco.org/156/AbstView_156_152360.html
Genomic profile and immune infiltrate in paired ovarian cancer (OC) samples pre- and post neoadjuvant chemotherapy (NC).

A TARGETED THERAPY INCREASES THE RATE OF HEALING IN BREAST CANCER

Dr. Suzette Delaloge, oncologist in the Department of Oncology Medicine and Head of the committee of breast pathology, leads at Gustave Roussy the ExteNET study, an international registering phase III multicentre and randomised study, which has included in total 2,821 patients with aggressive breast cancer but localised and which expresses the HER2 receiver.

The neratinib which is an inhibitor of tyrosine kinase pan-Her, was administered during 1 year as delayed adjuvant in women treated adequately according to the best current standards but whose cancer remains at risk of relapse. Patients will be followed for 5 years.

The first results, very positive, and after two years of follow-up, show a significant decrease of 33% of the risk of relapse of invasive breast cancer (main criterion of the study). It is for the first time the proof-of-concept of the fact that an inhibitor of tyrosine kinase is able to increase the rate of healing of a cancer and not only to prolong the survival in advanced stage of the disease.

Oral Presentation, Monday, June 1st, at 10h24 (Chicago time), room N Hall B1
Summary available on http://abstracts.asco.org/156/AbstView_156_149972.html
Neratinib after adjuvant chemotherapy and trastuzumab in HER2positive early breast cancer: Primary analysis at 2 years of a phase 3, randomized, placebocontrolled trial (ExteNET)

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THE GENITO-URINARY TUMOURS

STUDY THE MOLECULAR MECHANISMS ON TUMOURS FROM KIDNEY CANCER

Dr. Laurence Albiges, oncologist in the Department of oncology medicine, will present the results of the work on the various potential mechanisms of activation of the MET oncogene in the papillary carcinomas of the kidney.

It is an analysis carried out within the working group Kidney Renal Papillary (KIRP) of the broad program The Cancer Genome Atlas (TCGA). This project identified that 17% of tumours analysed relate an anomaly that can lead to a potential activation of the MET oncogene type enabling mutation, merger with another gene, or new transcribed gene inducing activation of the MET protein. These different modalities of activation seem to present a common phenotype.

This study has allowed us to highlight new mechanisms of activation of the MET oncogene and therefore the interest of this protein as a potential therapeutic target in kidney papillary cancer. Clinical trials are in progress to explore the role of MET inhibition in patients with kidney papillary metastatic cancer.

Poster, Monday June 1st, at 13h15 (Chicago time) room S Hall A, followed by a discussion on the same day at 16h45 (Chicago time), room E Arie Crown Theater.
Summary available on http://abstracts.asco.org/156/AbstView_156_150730.html
Distinct MET alterations induce a common phenotype and define a MET driven subset of papillary RCC: Results from the Cancer Genome Atlas (TCGA) Kidney Renal Papillary (KIRP) Working Group

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HOW TO MAKE DIFFERENCE BETWEEN A METASTATIC CANCER OF THE PROSTATE FROM A BAD DIAGNOSIS?

The results of three major clinical studies, French (GETUG 15), American (CHAARTED) and English (STAMPEDE which will be presented at ASCO 2015) converge and show that the addition of chemotherapy (Docetaxel) to the reference treatment (hormone) increases the overall survival of patients with cancer of the prostate of metastatic outset. These three studies will evolve the standard of treatment of the next few months.

In this context, a Collaboration conducted within the population of studies GETUG 15, and CHAARTED, led by Dr. Laurence Albiges,

The Prof. Christopher Sweeney (Dana-Farber Cancer Institute) and the Prof. Karim Fizazi, Head of the Department of Oncology Medicine, is committed to better define the most serious hormonodependants

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metastatic cancers, in order to be able to benefit to these patients of the new standard of treatment namely; the initiation of chemotherapy in addition to hormonal therapy.

Poster, Saturday, May 30th, at 13h15 (Chicago time), room S Hall A
Summary available on http://abstracts.asco.org/156/AbstView_156_150362.html
Disease burden and outcome in metastatic hormone sensitive prostate cancer (mHSPC).

Note: Dr. Bernard Escudier, oncologist in the Department of Oncology Medicine and responsible for the committee of genitourinary cancer at Gustave Roussy, will present a synthesis of abstracts on the targeted therapy and their targets in the kidney cancer on Monday, June 1st, at 17h21 room E Arie Crown Theater.

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