Highlights

GUSTAVE ROUSSY AT ASCO 2019

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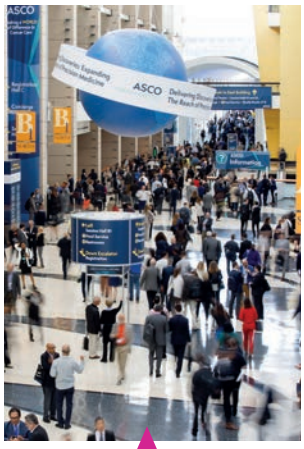
GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

GUSTAVE ROUSSY PRESENTATIONS AT ASCO 2019

As every year for almost 55 years, the world's leading cancer experts will meet in Chicago to talk about the latest advances in clinical oncology at the international meeting of the *American Society of Clinical Oncology* (ASCO). Naturally, Gustave Roussy will be one of the best represented institutions at this conference.

Apart from communication with their peers from around the world with the mutual benefits that represents, Gustave Roussy specialists will be participating in a total of 80 presentations (19 oral, 19 poster-discussions and 42 posters) chosen by the ASCO scientific committee. Two doctors from the Institute will also be discussants: Dr. Yohann Loriot on genito-urinary cancers and Pr. Benjamin Besse on lung cancers.

At this 55th annual meeting of the largest world oncology congress, Gustave Roussy will demonstrate its leading role in developing treatments such as immunotherapy and targeted therapy which are changing practice and transforming patient management. Patient quality of life during and after the experience of cancer remains an important and constant concern and is benefiting from the development of new technologies in that field.



ASCO

FROM 31 MAY TO 4 JUNE 2019

***American Society of Clinical Oncology* (ASCO)**
Chicago, Illinois
United States

ABOUT GUSTAVE ROUSSY

Gustave Roussy, leading cancer centre in Europe, covers the full range of expertise in the world of oncology and is totally committed to looking after patients. Its 3,100 professional staff are dedicated to patient care, research and teaching.

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1

IMMUNOTHERAPY
Long term benefits and evaluation of new agents

UROTHELIAL CANCER (BLADDER AND URINARY TRACT)
Long-lasting complete responses induced by immunotherapy

Urothelial cancer, usually developing in the bladder, is common and serious. Its management is complex. It accounts for 90% of bladder cancers. With 10,000 new cases diagnosed each year in France, bladder cancer is the urological cancer encountered most frequently after prostate cancer.

Up to the advent of the anti-PD1 and anti-PDL1 immunotherapies such as atezolizumab and pembrolizumab, which have shown themselves to be useful, oncologists' only option was to employ chemotherapy that was particularly toxic. These immunotherapies have now been approved in Europe for treatment of metastatic urothelial cancer but their cost is still not reimbursed in the French health system. An important question which doctors have still to resolve is the duration of tumour response and, in particular, that for complete response.

Dr. Yohann Loriot, oncologist specialised in bladder cancer, has led a joint analysis of the results of three studies evaluating atezolizumab. This shows that a complete response is found in about 10% of patients, occurring within the first eight months after commencing the agent. Complete response duration is long. The median for this is greater than two years in one of the studies and three years in the study with the longest follow-up. The great majority of patients who obtained a complete response are still alive several years after treatment was initiated.

Poster, presented Monday 3 June from 1:15 PM to 4:15 PM (Chicago time), Hall A
Durability of complete response (CR) with atezolizumab (atezo) in locally advanced/metastatic urothelial carcinoma (mUC)

▶ ***Abstract n°4527 to be read on***
https://meetinglibrary.asco.org/record/172212/abstract

IMMUNOTHERAPY AT GUSTAVE ROUSSY IN 2018 IS:

- **180 clinical trials open 14 of them sponsored by the Institute**
- **690 patients included in phase 1 to 3 clinical trials**

AT RISK MELANOMA

Benefits at 7 years of post-operative ipilimumab

Since 2015, ipilimumab has had FDA authorisation for post-operative use in melanoma patients. This was granted on the basis of clinical studies demonstrating a significant prolongation of relapse-free survival. Benefits of the agent have also been shown at more than 5 years of follow-up in relapse-free, metastasis-free and overall survival.

The results of the EORTC 18071 study presented at ASCO by Professor Alexander Eggermont, General Director of Gustave Roussy, show a benefit of post-operative ipilimumab treatment at 7 years when compared with placebo in patients at risk of metastatic melanoma. In such patients, ipilimumab significantly delays relapse and the appearance of metastases. It also prolongs overall survival. The benefits observed are of long duration and apply to all patients, regardless of sub-group.

Poster discussion, presentation Saturday 1 June from 8:00 AM to 11:00 AM (Chicago time), Hall A, followed by discussion from 1:15 PM to 2:45 PM, Hall D1
Ipilimumab versus placebo after complete resection of stage III melanoma: Long-term follow-up results the EORTC 18071 double-blind phase 3 randomized trial

Abstract n°2512 to be read on
https://meetinglibrary.asco.org/record/172423/abstract

MELANOMA

Immunological-type adverse effects of post-operative pembrolizumab treatment are associated with a better prognosis

Findings of previous studies suggested that patients with immunological adverse effects (inflammatory lung disease, colitis, hepatitis, nephritis, etc.) responded better to immunotherapy than the other patients but this had not been clearly demonstrated up till this time.

In the EORTC 1325/KEYNOTE-054 trial comparing pembrolizumab with placebo, medical researchers sought to establish a connection between these adverse effects and relapse of patients having surgery for metastatic melanoma at high risk of relapse. More than 1,000 patients were included in this double-blind multicentre trial.

The study results presented by Professor Alexander Eggermont, Gustave Roussy General Director, show for the first time that the occurrence of immunological adverse effects is associated with delay in relapse and that the prolonged use of corticosteroids (30 days or more) to control these adverse effects increases the risk of relapse.

Poster discussion, presentation Saturday 1 June from 8:00 AM to 11:00 AM (Chicago time), Hall A, followed by discussion from 1:15 PM to 2:45 PM, Hall D1

Prognostic and predictive value of an immune-related adverse event among stage III melanoma patients included in the EORTC 1325/KEYNOTE-054 pembrolizumab versus placebo trial.

▶ ***Abstract n°2517 to be read on***
https://meetinglibrary.asco.org/record/172428/abstract

SINCE 2013
a total of almost 3,400 patients treated with immunotherapy in a clinical trial

GYNAECOLOGICAL CANCERS

Promising results of a targeted immunotherapeutic agent tested for the first time in the human

Gynaecological cancers have not yet benefited from the rapid development of immunotherapeutic agents targeting PDL1 or PD1. It seems to be necessary to find more innovative immunotherapeutic approaches, appropriate to the biological characteristics of these tumours. GM102 is a novel immunotherapeutic agent which targets both a receptor located on the surface of gynaecological tumour cells (AMRH2) and an immune cell receptor (CD16 on macrophages). The objective is to increase the ability of these macrophages to destroy tumour cells.

An international trial testing this novel immunotherapeutic agent for the first time in the human has been coordinated by Dr. Alexandra Leary, gynaecological specialist oncologist and Inserm researcher, in collaboration with GamaMabs, a French immuno-oncology biotech company. The patients treated with this new agent had epithelial ovarian, endometrial or cervical cancer or a granulosa cell tumour. The medication was very well tolerated both as monotherapy and combined with carboplatin and taxol [paclitaxel].

Used as monotherapy a response was obtained in a patient with a rare cancer, granulosa cell tumour, for which no targeted therapy is available.

Combined with chemotherapy, 44% of the patients, energetically pre-treated with chemotherapy, had a reduction in tumour mass. These encouraging results justify future trials of GM102 combined with standard treatment or immunotherapy in order to increase the potential anti-tumour effects.

Poster discussion, presentation Saturday 1 June from 8:00 AM to 11:00 AM (Chicago time), Hall A followed by discussion from 1:15 PM to 2:45 PM, Hall D1

First-in-human first-in-class phase I trial of murlentamab, an anti-Mullerian-hormone receptor II (AMHRII) monoclonal antibody acting through tumor-associated macrophage (TAM) engagement, as single agent and in combination with carboplatin (C) and paclitaxel (P) in AMHRII-expressing advanced/metastatic gynecological cancer patients (pts).

▶ ***Abstract n°2521 to be read on***
https://meetinglibrary.asco.org/record/172432/abstract

2

TARGETED THERAPIES
Long-term prolonged responses and novel, more precise targets with a more strategic role in the development of cancers

MELANOMA
The benefits of dual targeted therapy confirmed at five years

The treatment of patients with metastatic melanoma with the BRAF V600 mutation, using combined dabrafenib and trametinib, two anti-cancer agents which target an intracellular signalling pathway specifically involved in the cancer process, prolongs progression-free survival and improves overall survival in many patients. These are the latest results, at five years, confirming the value of this targeted dual therapy. These results, presented at the ASCO meeting and published simultaneously in the *New England Journal of Medicine*, are derived from a combined analysis of the COMBI-d and COMBI-v studies, led, in particular, by Professor Caroline Robert, Head of the Dermatology Department at Gustave Roussy.

The first combined results of these two trials, analysed at 3 years and published in 2017, showed that disease had not progressed in 23% of patients and that 44% remained alive. In this latest study, the benefits of this targeted dual therapy at 4 and 5 years are confirmed.

"Presentation and publication of the results of this study demonstrate the long-term benefits of a combination of two targeted therapies at a time when this approach to cancer therapy is being neglected somewhat in favour of immunotherapy," commented Professor Robert.

Oral presentation, Tuesday 4 June from 11:57 AM to 12:09 PM (Chicago time), Room S406
Five-year analysis on the long-term effects of dabrafenib plus trametinib (D + T) in patients with BRAF V600–mutant unresectable or metastatic melanoma.

▶ ***Abstract n°9507 to be read on***
https://meetinglibrary.asco.org/record/174754/abstract

PAEDIATRIC CANCERS

Larotrectinib, first targeted therapy for childhood solid tumours

Three studies on larotrectinib, conducted in partnership with Gustave Roussy and presented at ASCO, show the importance of this selective TRK inhibitor both in childhood and adult oncology. Larotrectinib is the first agent capable of selectively blocking TRK fusions, genetic abnormalities implicated in a number of cancers, most particularly rare cancers in adults and children. They arise early in the development of the cancer and remain present up to its possible dissemination. Their action involves sending signals that stimulate growth of cancer cells.

Concomitantly, the results of the international MAPPYACTS trial, also presented at ASCO and led by Gustave Roussy in France, Ireland and Italy, show that sequencing of tumours in children in relapse or with a failure of therapy can lead to the identification of young patients likely to benefit from larotrectinib treatment.

This drug has already been authorised in the United States, where it is indicated for adult and paediatric tumours with TRK fusions, regardless of tumour type. As such, it is the first targeted therapy to be authorised for an "agnostic" indication. The European Medicines Agency is currently examining an application. In France, while awaiting marketing authorisation, this agent has been available for some weeks and can be used under a cohort authorisation for temporary use arrangement. It should, therefore, soon become the first targeted therapy authorised for treatment of solid tumours in children.

500 children and adolescents had their tumour sequenced in the MAPPYACTS study

Poster discussion, presented Saturday 1 June from 8:00 AM to 11:00 AM (Chicago time), Hall A followed by discussion from 1:15 PM to 2:45 PM, Room S504
Can pediatric and adolescent patients with recurrent tumors benefit from a precision medicine program? The European MAPPYACTS experience

▶ ***Abstract n°10018 to be read on***
https://meetinglibrary.asco.org/record/170955/abstract

Oral presentation, Sunday 2 June from 8:12 AM to 8:24 AM (Chicago time), Room S504
Larotrectinib efficacy and safety in pediatric TRK fusion cancer patients

▶ ***Abstract n°10010 to be read on***
https://meetinglibrary.asco.org/record/170953/abstract

Oral presentation, Monday 3 June from 3:15 PM to 3:27 PM (Chicago time), Room S102
Activity of larotrectinib in TRK fusion cancer patients with brain metastases or primary central nervous system tumors

▶ ***Abstract n°2006 to be read on***
https://meetinglibrary.asco.org/record/174568/abstract

Poster, presented Saturday 1 June from 1:15 PM to 4:15 PM (Chicago time), Hall A
Patient-reported outcomes from two global multicenter clinical trials of children and adults with tropomyosin receptor kinase (TRK) fusion cancer receiving larotrectinib

▶ ***Abstract n°6602 to be read on***
https://meetinglibrary.asco.org/record/176143/abstract

DIGESTIVE TRACT CANCERS - GIST (STROMAL GASTROINTESTINAL TUMOURS)

Nearly 100% level of disease control in certain patients with a new targeted therapy

The GIST are rare tumours (900 cases per year in France). They may arise at any point in the digestive tract (oesophagus, stomach, small intestine, colon and rectum). Three drugs are approved at present for treatment of inoperable or metastatic GIST bearing a KIT gene mutation: imatinib (1st line), sunitinib (2nd line) and regorafenib (3rd line). No other drug has marketing authorisation.

Less often, the GIST may possess a "D842V" mutation of the PDGFRA gene (about 20% of stomach GIST). These tumours are resistant to all currently marketed drugs.

Avapritinib is a highly specific agent targeting KIT mutations that are resistant to other available drugs. It also targets "D842V" mutations of the PDGFRA gene.

In the phase 1 NAVIGATOR study, Dr. Olivier Mir, oncologist specialised in sarcomas at Gustave Roussy, and colleagues from European and North American expert centres have evaluated the safety and efficacy of avapritinib administered orally in patients with GIST.

In this phase 1 study and in its extension cohorts, involving 237 patients, avapritinib was particularly well tolerated with a side effect profile similar to that of imatinib (standard 1st line therapy), including memory impairment (29% of patients). Only 10% of the patients (those, however, having been energetically pre-treated) had to stop their medication because of an adverse event.

In GIST patients with the KIT mutation, the objective response rate was 22% (compared with < 10% for sunitinib and regorafenib). 54% of patients had their disease stabilised, so the value for disease control was 76%. In GIST patients with the D842V mutation of the PDGFRA gene the objective response rate was 84%, and 14% of the patients had their disease stabilised, thus giving a disease control rate of 98% (only a single patient with GIST PDGFRA D842V harboured disease resistant to avapritinib from the outset).

This study was conducted at Gustave Roussy within the Drug Development Unit (DITEP) directed by Dr. Christophe Massard. These results will lead to a marketing authorisation request to the FDA. An article reporting the NAVIGATOR study findings has, in addition, been submitted for publication to the prestigious *New England Journal of Medicine*.

Poster discussion, presented Saturday 1 June from 8:00 AM to 11:00 AM (Chicago time), Hall A, followed by discussion from 3:00 PM to 4:30 PM, Room S404
Clinical activity of avapritinib in ≥ fourth-line (4L+) and PDGFRA Exon 18 gastrointestinal stromal tumors (GIST)

▶ ***Abstract n°11022 to be read on***
https://meetinglibrary.asco.org/record/174900/abstract

GUSTAVE ROUSSY DRUG DEVELOPMENT DEPARTMENT performs half of all early clinical trials in France

ADVANCED LUNG CANCER

A new conjugated antibody demonstrates its role for the first time in man

A phase 1 trial evaluated safety and efficacy of SAR408701, a new agent, in patients with locally advanced solid tumours. This is an anti-CEACAM5 conjugated antibody. The results presented at ASCO were obtained in patients with locally advanced lung cancer shown histologically not to be squamous cell in type. The tumour cells over-expressed CEACAM5 (CEA related cell adhesion molecule), which is expressed on the surface of several types of cancer cells.

The principal objective of this trial, presented at ASCO by Dr. Anas Gazzah, oncologist in the Gustave Roussy Drug Development Department, was to define the toxic effects and the degree of response. The secondary objectives concerned the safety and the pharmacokinetics. SAR408701 was administered intravenously every two weeks at the maximum tolerated dose of 100 mg/m2, and assessments were performed at 8 week intervals.

A total of 38 patients with advanced carcinoma of lung over-expressing CEACAM5 were treated with SAR408701. The overall response rate was 25%; 25% of the patients had a partial response and 37.5% disease stability. The principal adverse effects were corneal involvement (39.5%) of which 23.7% represented keratitis, dyspnoea (31.6%), and diarrhoea (26.3%). SAR408701 was well tolerated overall with the keratopathies being reversible with cessation of treatment or using reduced doses still having anti-tumour effects.

Poster, presented Sunday 2 June from 8:00 AM to 11:00 AM (Chicago time), Hall A
First-in-human phase 1 study of the antibody-drug conjugate (ADC) SAR408701 in advanced solid tumors: Dose-expansion cohort of patients (pts) with non-squamous non-small cell lung cancer (NSQ NSCLC)

▶ ***Abstract n°9072 to be read on https://meetinglibrary.asco.org/record/174900/abstract***

DRUG DEVELOPMENT DEPARTMENT leads the largest early trials clinical research programme in Europe

3

QUALITY OF LIFE DURING AND AFTER CANCER
New technologies and advances in therapy to help the patient

BREAST CANCER
Artificial intelligence can predict the risk of post-treatment fatigue

Research results presented at the 2019 ASCO Conference show for the first time that artificial intelligence can help predict the chances of development of severe fatigue in women due to undergo treatment for breast cancer. This is before they commence treatment and even before they show clinical symptoms associated with such asthenia.

More than a quarter of patients experience severe fatigue in the months following completion of breast cancer treatment. Gustave Roussy medical researchers in collaboration with colleagues at the Memorial Sloan-Kettering Cancer Center tried to develop a test which can recognise at the time of diagnosis of breast cancer, before institution of treatment, which women are likely to be affected by fatigue. The aim is to recommend, within the bounds of the possible, alternative, better-tolerated therapies.

The researchers used patients from the CANTO (CANcer TOxicities) cohort, sponsored by Unicancer and coordinated by Professor Fabrice André, Inserm Research Director and Gustave Roussy oncologist with a special interest in breast cancer. The study demonstrates the value of exploring the possibilities that artificial intelligence may offer for curing breast cancer while restricting the possible sequelae to a minimum.

Oral presentation, Saturday 1 June from 8:36 AM to 8:48 AM (Chicago time), Room S102
Prediction of treatment (tx)-induced fatigue in breast cancer (BC) patients (pts) using machine learning on genome-wide association (GWAS) data in the prospective CANTO cohort.

▶ ***Abstract n°11515 to be read on***
https://meetinglibrary.asco.org/record/174965/abstract

CANTO COHORTE:
12,000 women
26 centres in France
Unicancer sponsorship

CANCER OF THE PROSTATE

Darolutamide reduces the risk of pain and does not worsen the quality of life in patients treated for prostate cancer

Darolutamide is a new androgen-receptor inhibitor, these steroid hormones (androgens) being implicated in the genesis of prostate cancer. It reduces the incidence of pain and does not worsen the quality of life in patients treated for non-metastatic prostate cancer, according to the results of the ARAMIS study. Presented at the ASCO meeting by Professor Karim Fizazi, principal investigator for the trial and oncologist specialised in prostate cancer, the findings demonstrate the value of this drug which increases patient survival for those without disseminated disease by almost two years.

"In addition to an improvement in metastasis-free survival, a good safety profile is a major feature for these patients (the great majority being asymptomatic) with prostate cancer that has become resistant to hormone therapy. The choice of therapeutic agent may impinge on their general well-being and adherence to treatment with the agent and with other drugs being taken concomitantly," summarised Professor Fizazi.

The drug was developed for use in men with non-metastatic disease who had received local treatment and who had become resistant to standard hormone therapy. Its safety and efficacy were evaluated in the ARAMIS study, a phase 3 placebo-controlled trial. **The results were presented in February of this year at the ASCO genitourinary cancer meeting** in San Francisco and published simultaneously in the *New England Journal of Medicine*. The researchers continued to analyse the data in order to evaluate various factors influencing tolerance as well as quality of life for the patients treated.

Oral presentation, Friday 31 May from 2:45 PM to 2:57 PM (Chicago time), Arie Crown Theatre
Impact of darolutamide (DARO) on pain and quality of life (QoL) in patients (Pts) with nonmetastatic castrate-resistant prostate cancer (nmCRPC).

▶ ***Abstract n°5000 to be read on***
https://meetinglibrary.asco.org/record/172909/abstract

METASTATIC PROSTATE CANCER

Offering patients the choice when two therapies with similar efficacy are available?

Two taxanes, docetaxel and cabazitaxel, are the reference treatments in men with metastatic prostate cancer that has become resistant to hormone therapy. The FISRTANA clinical trial showed that their efficacy was similar. Medical researchers at Gustave Roussy therefore sought to evaluate patient preference between the two taxanes.

Gustave Roussy promoteur

In the CABADOC trial sponsored by Gustave Roussy, patients who had never received taxanes and whose metastatic prostate cancer had become resistant to hormone therapy were allocated randomly between the two arms of the study. Those in the first arm received 4 courses of docetaxel first, followed by four courses of cabazitaxel (DO-CA); the patients in the second arm received the drugs in the reverse order (CA-DO). Patient preferences for one or other taxane were assessed using questionnaires completed by those who had received at least one cycle of each taxane and whose disease had not progressed since the first one.

This phase 3 clinical study recruited 195 men from 17 centres between June 2014 and October 2016. The results, presented by Dr. Giulia Baciarello, Gustave Roussy oncologist specialised in prostate cancer, showed that patients preferred cabazitaxel (43%) to docetaxel (27%). Only 30% of the patients professed no preference.

Poster Discussion, presented Saturday 1 June from 1:15 PM to 4:15 PM (Chicago time), Hall A, followed by discussion from 4:30 PM to 6:00 PM, Arie Crown Theatre
Final results from the randomized CABADOC trial: Patient preference between cabazitaxel and docetaxel for first-line chemotherapy in metastatic castrate-resistant prostate cancer (mCRPC)

▶ ***Abstract n°5017 to be read on***
https://meetinglibrary.asco.org/record/174934/abstract

FURTHER INFORMATION

on the presence of Gustave Roussy at ASCO

www.gustaveroussy.fr/en/asco2019

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