GUSTAVE ROUSSY PRESENTS PROMISING RESULTS IN PAEDIATRIC ONCOLOGY

At this 52nd annual ASCO Conference, paediatric trials conducted at Gustave Roussy are in the spotlight. The Institute’s physician-researchers are presenting 10 studies, 5 as oral presentations and 5 as posters. This research work studies the use of a number of drugs administered alone or in combination in a variety of diseases, thus contributing to the establishment of new standard treatment regimens. Gustave Roussy is a leader on the international stage, driving advances in therapy and in paediatric oncology.

The Institute’s commitment to curing more patients and doing so better is shown in particular by public-private collaboration in a trial sponsored by Gustave Roussy. This is presented by Dr. Véronique Minard-Colin, Paediatric Oncologist in the Gustave Roussy Childhood and Adolescent Oncology Department. This trial aims to improve survival in patients with Burkitt’s lymphoma by using treatment combining conventional chemotherapy and immunotherapy. Dr. Jacques Grill, Paediatric Neuro-Oncologist in the Gustave Roussy Childhood and Adolescent Oncology Department, will present a phase I trial, also sponsored by the Institute, exploring the use of a promising therapeutic combination of chemotherapy and targeted therapy in low-grade glioma.

Three early clinical trials demonstrate that Gustave Roussy is in the forefront of offering the youngest cancer patients access to the latest therapies. These trials are led by Dr Birgit Geoerger, Paediatric Oncologist in the Gustave Roussy Childhood and Adolescent Oncology Department. For the first time novel therapies which have been shown to be effective in the adult are being tested in the child and adolescent. In addition, at a session devoted to precision medicine, Professor Gilles Vassal, Director of Clinical Research at Gustave Roussy will present the Acsé crizotinib paediatric trial sponsored by UNICANCER. This trial aims to target therapy for patients according to the genomic profile of their tumours.

It should also be noted that Dr. Dominique Valteau-Couanet, Head of the Gustave Roussy Childhood and Adolescent Oncology Department, will be participating as a discussant in a plenary session at which the assessment and discussion of a trial conducted in the United States on childhood neuroblastoma will be assessed and discussed.
A PROMISING COMBINATION OF CHEMOTHERAPY AND TARGETED THERAPY IN ADVANCED BURKITT’S LYMPHOMA

Dr Véronique Minard-Colin is presenting very good results from intermediate analysis of data in the inter-B-NHL ritux 2010 international, phase III, randomised clinical trial. This academic trial is sponsored by Gustave Roussy and conducted in collaboration with the Children Oncology Group (COG), the European intergroup For Childhood NHL (EICNHL) and Roche Laboratories.

“We have almost won the battle against this disease. Since the 1980s our cure rate has risen from 30% to more than 80% with chemotherapy alone”, declared Dr. Catherine Patte, Medical Oncologist in the Gustave Roussy Childhood and Adolescent Oncology Department and principal investigator in this international trial. The combined regimen tested in this trial increased the survival rate by more than 10% in children with advanced leukaemia or advanced Burkitt’s lymphoma.

This study aimed to compare the results of treatment of patients with rituximab, a monoclonal antibody directed against CD20 (expressed on the surface of tumour cells), combined with the standard chemotherapy prescribed for this condition with those in patients treated with standard chemotherapy alone. 310 children participated in the trial. The results showed a 70% reduction in the risk of events (death, relapse, progression, second cancer, etc.) for combined therapy versus chemotherapy alone.

These very good results led the Data Monitoring Committee to recommend that randomisation should cease, so that all the patients with advanced disease (around 60% of patients) can benefit from the rituximab-chemotherapy combination. This is becoming the new standard therapy for these patients with the worst prognosis (this is not the case for those patients in the standard risk category in whom the cure rate with chemotherapy alone is over 98% with no long-term sequelae).

EURO-EWING 99 STUDY: EWING’S SARCOMA AT HIGH RISK OF RELAPSE. TOWARDS A NEW STANDARD TREATMENT

Chemotherapy is an essential component in the treatment of Ewing’s sarcoma, a cancer of bone. This is an uncommon tumour which mainly affects adolescents and young adults. EURO-EWING 99 is a large international study conducted by European research groups. It includes the R2Loc and R2Pulm phase III randomised trials in which Busulfan-Melphalan at high dose is compared with
conventional treatment. The R2Loc trial assessed the efficacy and safety of high dose chemotherapy on survival without an event and overall survival in patients with localised Ewing's sarcoma at high risk of relapse. After 7 cycles of identical chemotherapy in the 2 patient groups, patients were then assigned either to Busulfan-Melphalan or to VAI (vincristine, actinomycin D, ifosfamide) standard chemotherapy.

If the eligibility criteria were adhered to well, the Busulfan-Melphalan combination produced a substantial, significant reduction in the risk of relapse and death with an acceptable side effect profile. Thus, survival without relapse was significantly higher in the BuMel patients compared with those on VAI: 67% versus 53% at three years with the difference maintained beyond three years. Overall survival was also significantly helped by BuMel: 78% versus 70% at three years.

These results show that BuMel should become the new standard treatment in patients with localised Ewing sarcoma at high risk of relapse, in the absence of a contra-indication such as the need for irradiation of the spinal cord or a large portion of the gastrointestinal tract. The R2Pulm trial involved Ewing sarcoma patients with pulmonary (but no other) metastases. After 7 cycles of identical chemotherapy in the 2 patient groups, patients were then assigned either to Busulfan-Melphalan or to standard chemotherapy followed by pulmonary radiotherapy. The data do not show any clear benefit in favour of high dose chemotherapy without pulmonary radiotherapy compared with standard chemotherapy combined with radiotherapy to the lungs.

The French investigators from the Société Française des Cancers et Leucémies de l’Enfant (SFCE) [French Society for Childhood Cancer and Leukaemia], from the UNICANCER Sarcoma group and from GSF-GETO (French Sarcoma Group – Group for the Study of Bone Tumours) were closely involved in the design of these trials and the main contributors to this international programme. 477 patients from 15 European countries and the United States were recruited (31% of these from France for R2Loc and R2Pulm).

UNICANCER sponsored the trial in France. Dr. Odile Oberlin and then Nathalie Gaspar of the Childhood and Adolescent Oncology Department were the French coordinators and Dr. Marie Cécile Le Deley, Paediatric Statistician in the Department of Biostatistics and Epidemiology, organised the data handling and performed the statistical analyses. This programme was supported in France by La Ligue nationale contre le cancer (National Cancer League), the Fédération Enfants et Santé (Children and Health Federation) and the SFCE. The EURO-EWING 99 programme shows how close...
ACSE CRIZOTINIB TRIAL: CHOOSING A TARGETED THERAPY AFTER TUMOUR GENOMIC ANALYSIS

Professor Gilles Vassal, principal investigator, is presenting the findings of the paediatric cohort in the AcSé crizotinib trial. The AcSé crizotinib programme was designed to allow patients (children, adolescents or adults) access to crizotinib, a targeted therapy. This is given to patients in a situation of therapeutic failure where the tumour bears a genetic abnormality in at least one of the crizotinib targets (ALK, MET or ROS1).

It is sponsored by UNICANCER and coordinated scientifically by Professor Gilles Vassal. It is the first trial to be launched in the INCa (National Cancer Institute) AcSé programme.

A tumour molecular portrait was obtained for 107 children. 18 had a tumour with one of the crizotinib targets (ALK, ROS or MET). Of the 11 children with failed therapy of malignant tumours, aged from 3 to 16 years, who participated in the trial, 5 had a tumour response which lasted more than 6 months.
THREE CLINICAL TRIALS TESTING NOVEL THERAPIES IN THE CHILD FOR THE FIRST TIME
Dr. Birgit Geoerger participated in three phase I clinical trials testing for the first time in children novel therapeutic agents which had been shown to work in adults:

- One of these, led by Dr. Geoerger, was the KEYNOTE-051 phase I/II trial in which young patients with advanced melanoma or advanced lymphoma which was refractory or in relapse, received pembrolizumab (pembro), a monoclonal anti PD1 antibody. This agent is used in adults with advanced melanoma or advanced lymphoma and its anti-tumour activity has been demonstrated.
  Abstract n°TPS10585

- A phase I/II trial testing nab-paclitaxel, a chemotherapeutic agent, in young patients with recurrent or refractory solid organ tumours. The recommended dose was used and good results were obtained both for clinical effectiveness and safety in use. Professor Gilles Vassal is the last author of this presentation.
  Abstract n°10551

- A phase I trial testing regorafenib, a targeted therapy, in young patients with recurrent or refractory solid organ tumours. The agent was well tolerated at the recommended dose.
  Abstract n°10542

VINILO STUDY COMBINING VINBLASTINE AND NILOTINIB IN LOW-GRADE GliOMA
In a phase I clinical trial, Dr. Jacques Grill, Paediatric Neuro-Oncologist in the Gustave Roussy Department of Childhood Oncology, studied the efficacy and safety of treatment with a combination of nilotinib, a targeted therapy, and vinblastine chemotherapy (VINILO), in 35 young patients with low-grade glioma in relapse after conventional treatment.

The objective was to determine the dosages of VINILO to be employed in a subsequent phase II trial. Low-grade glioma is the commonest brain cancer seen in children. These often relapse.
VINILO is a European therapeutic trial sponsored by Gustave Roussy. The fact that long-lasting responses have been observed and that tolerance is good justifies further assessment of this combination in a comparative trial which is due to start in the summer and will be extended to other European countries.

TO FIND OUT MORE:
read the abstract n° 10555

Dose-finding study of vinblastine in combination with nilotinib in children, adolescents and young adults with refractory or recurrent low-grade gliomas: Results of the ITCC/SIOPE-Brain VINILO phase I trial (NCT 01887522).
Authors: Jacques / Grill, Marie-Cecile Le Deley, Gwenael / Le Teuff, Samuel / Abbou, Birgit Geoerger, Francisco Baustista, Katly Malekzadeh, Angelo Paci, Emilie De Carli, Anne-Isabelle Berthozi, Anne Pagnier, Pierre Leblond, Frederic / Millot, Isabelle Aerts, Christelle Dufour, Claire Berger, Panny Fouogo, Karsten Nysom, Gilles Vassal

VINILO STUDY COMBINING VINBLASTINE AND NILOTINIB IN LOW-GRADE GliOMA

In a fourth phase II study, bevacizumab was combined with chemotherapy in children with metastatic rhabdomyosarcoma or non-rhabdomyosarcoma soft-tissue sarcoma. The safety profile was acceptable and there was an improvement in tumour response but not in progression-free survival.
Abstract n°11054


June 3-7, 2016
McCormick Place / Chicago, Illinois
ASCO2016
GUSTAVE ROUSSY, LEADING COMPREHENSIVE CANCER CENTER IN EUROPE, AT ASCO ANNUAL MEETING

At this 52nd annual meeting of the world’s most important oncology conference, Gustave Roussy will confirm its leading role in the development of three therapeutic strategies that are changing practice and transforming patient treatment. Immunotherapy, which is extending its application to new conditions, and precision medicine are becoming routine therapeutic options. This 2016 meeting will also be noteworthy for throwing light on the optimisation of existing treatments, as reflected by the presentation in plenary session of childhood neuroblastoma treatment, for which Dr Dominique Valteau-Couanen, Head of the Gustave Roussy Paediatric Department, will be a discussant.

This year, Gustave Roussy medical researchers will be revealing their work in a total of 75 presentations. The ASCO Scientific Committee has selected 21 oral communications, 6 of which will be delivered by doctors from the Institute; 11 poster-discussions, 6 of which are to be presented by Gustave Roussy researchers; and 42 posters and 1 educational session authored by doctor researchers from the Institute. Gustave Roussy is the sponsor of four clinical trials, the results of which will be communicated during the conference.