CONCOMITANT MUTATIONS OF SEVERAL ONCOGENIC PATHWAYS ARE COMMON IN HIGH RISK ENDOMETRIAL CANCERS

Gustave Roussy’s medical researchers will be presenting their clinical and translational research papers at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO), the world’s biggest oncology gathering. This year there will be 18 oral papers presented by the Institute’s physician-researchers, including 10 on work carried out and 37 posters.
Dr Alexandra Leary and Dr Catherine Lhomme presented a study concerning the molecular analysis of the tumour genome of patients suffering from endometrial cancer at an advanced or recurrent stage on Monday June 2nd at the 50th ASCO Congress in Chicago, at the Gynecology Poster Highlights session. This study shows that in these high risk patients, several mutations frequently co-exist on different genes involved in parallel oncogenic pathways. This would explain the disappointing results obtained in targeted therapeutic trials with monotherapy. This study shows the benefit of undertaking trials testing combinations of target compounds corresponding to identified mutations.

IDENTIFICATION OF CONCOMITANT MUTATIONS IN HIGH RISK ENDOMETRIAL CANCERS

Endometrial cancer is the most frequent pelvic gynecological cancer in France. It usually occurs after the menopause and is the 5th most common cancer in women.

The majority of patients have a histologically favorable endometrial cancer (low grade endometrioid) at an early stage and will be cured by local treatment alone. But the risk of recurrence is greater for patients with an unfavorable histology or at an advanced stage. Up to now, genomic studies mainly included tumours with early stage good prognosis endometrial cancers.

For this study, samples from patients with high-risk endometrial cancers were identified in the Gustave tumour bank.

Sixty nine samples corresponding to 54 patients suffering from endometrial cancer with a high risk of recurrence or relapse were selected. In 13 patients, samples from the primary tumour and from metastatic sites were available.
Samples underwent genetic sequencing. This involved 79 exons from 13 genes (KRAS, NRAS, HRAS, BRAF, AKT1, PIK3CA, PIK3R1, PIK3R2, PTEN, STK11, ESR1, TP53, FGFR2). These genes are implicated in oncogenesis and are potentially "targetable" with therapies undergoing development.

The results have shown that 80% of patients had at least one mutation. The commonest was TP53 in 35% of patients. Changes in the PI3K pathway have been identified in 65% of patients and the RAS mutation in 24%. Sixty five percent of patients moreover were carriers of simultaneous mutations in several oncogenic signalization pathways.

Finally, among the 13 patients with metastases, 38% of metastases showed different mutations from the primary tumour.

Simultaneous actionable oncogenic mutations are therefore frequent in high risk or recurrent endometrial cancer.

A focused strategy only targeting one single genetic abnormality is unlikely to be effective for these patients.

This study provides the rationale for clinical trials investigating the combined inhibition of PI3K and MEK, PI3K and FGFR or MEK and FGFR in genomically patients with endometrial cancer.

BRACHYTHERAPY

Brachytherapy is an irradiation technique which consists of introducing radioactive sources in contact with or even placed directly into the tumour. This treatment directly targets the area involving the cancer. Gustave Roussy has considerable experience in brachytherapy.

Currently approximately 250 patients are treated each year using this method in cancers of the bronchus, esophagus, cancers of a gynecological origin and, in the future, in cancers of the prostate. Gustave Roussy is also participating in the treatment of coronary restenosis using this method providing support for cardiologists. The Institute has an innovative technical capacity equipped with 6 curietrons.

A new brachytherapy approach is practiced at Gustave Roussy; this is pulsed brachytherapy, an innovative method of fractionated radiation.