PRESS RELEASE

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THE LANCET

A CLINICAL TRIAL PROVES THE EFFICACY OF SUNITINIB IN THE TREATMENT OF RARE NEUROENDOCRINE TUMORS

Led by Dr. Éric Baudin, head of Gustave Roussy's endocrine tumors committee, the European trial FIRSTMAPP is the first-ever randomized clinical trial concerning phaeochromocytomas and paragangliomas, rare neuroendocrine tumors. The results, published in February 2024 in *The Lancet,* show the efficacy of sunitinib, a tyrosine kinase inhibitor.
Patients affected by an ultra-rare disease have difficulties accessing medical innovations, mostly because it can be hard to recruit a satisfying amount of patients to run clinical trials. FIRSTMAPP illustrates the key role of research in rare diseases and confirms the world-renowned expertise of Gustave Roussy in rare tumors.
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Metastatic progressive phaeochromocytomas and paragangliomas (PPM) are tumors located in the chromaffin tissue, which can be found in the adrenal glands or paraganglions. In the majority of cases, these tumors are benign and heal after surgery. However, for 10% of patients, they are malignant and can progress and metastasize. Metastatic progressive phaeochromocytomas and paragangliomas are ultra-rare cancers, with an annual incidence of less than one in a million. In 30% of cases, the cause is hereditary.

Before the FIRSTMAPP study, no randomized controlled trial had ever been done on patients with this type of cancer. The two historical treatments are meta-iodobenzylguanidine therapy, a 131-iodine-labeled analog of the norepinephrine transporter, and dacarbazine-based cytotoxic chemotherapy. However, no systemic treatment has ever been standardized, and the rate of complete response is extremely rare. Partial responses concern only 25% of patients.

Tyrosine kinase inhibitor

The FIRSTMAPP trial, promoted by Gustave Roussy and led by Dr. Éric Baudin, is a multicenter, international, randomized, placebo-controlled, double-blind, phase 2 trial done at 14 academic centers across four European countries between 2011 and 2019.

Its goal was to evaluate the safety and effectiveness of sunitinib, a tyrosine kinase inhibitor, among patients with metastatic progressive phaeochromocytomas and paragangliomas, after initial preclinical studies had shown a possible benefit of this molecule. Tyrosine kinase is an enzyme,

which plays a role in cell development and division. Treatments with tyrosine kinase inhibitor can therefore help prevent tumor growth.

Despite the scarcity of metastatic progressive phaeochromocytomas and paragangliomas in the global population, a satisfying number of patients had been recruited to take part in the FIRSTMAPP trial, suffering from a sporadic or inherited pathology, thanks to the prior structuring of the French ENDOCAN-COMTE and European ENSAT networks, which manage these patients.

Between December 2011 and January 2019, 78 participants – 46 men and 32 women – were randomized to sunitinib (37.5 mg daily) or placebo. Of these 78 patients, 25 had an abnormality in the SDHB gene (a risk factor for malignancy and poor prognosis), and 54 had already received another therapy before starting the clinical trial.

Randomization was stratified according to SDHB gene abnormality and the number of previous systemic treatments. The primary endpoint was progression-free survival at 12 months.

The importance of the SDHB mutation

The results achieved met the primary objective, with progression-free survival at 12 months in 36% of patients in the sunitinib group, versus 19% in the placebo group. Among patients with an SDHB gene mutation, FIRSTMAPP reported a tumor response rate of 50%, the highest in the literature for endocrine tumors treated with sunitinib.

"FIRSTMAPP positions sunitinib as the treatment with the highest level of evidence in patients with progressive metastatic pheochromocytoma/paraganglioma, and even more so in patients whose tumors carry a mutation in the SDHB gene. This latest result validates a personalized approach based on the consequences of this gene mutation" concludes Éric Baudin, MD, Ph.D.

The study was carried out thanks to grants from the PHRC in France, the Horizon 2020 program, the German Ministry of Research, Pfizer laboratory, and a private donor.

Source
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Background on Gustave Roussy

Ranked as the leading French and European Cancer Centre and fourth in the world, Gustave Roussy is a centre with comprehensive expertise and is devoted entirely to patients suffering with cancer. The Institute is a founding member of the Paris Saclay Cancer Cluster. It is a source of diagnostic and therapeutic advances. It caters for almost 50,000 patients per year and its approach is one that integrates research, patient care and teaching. It is specialized in the treatment of rare cancers and complex tumors and it treats all cancers in patients of any age. Its care is personalized and combines the most advanced medical methods with an appreciation of the patient's human requirements. In addition to the quality of treatment offered, the physical, psychological and social aspects of the patient's life are respected. 4,100 professionals work on its two campuses: Villejuif and Chevilly-Larue. Gustave Roussy brings together the skills, which are essential for the highest quality research in oncology: 40% of patients treated are included in clinical studies.
For further information**: www.gustaveroussy.fr/en, Twitter, Facebook, LinkedIn, Instagram**

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