

## PARKINSON'S DISEASE

**A treatment for diabetes may slow the progression of Parkinson's disease: an innovation for which the world has been waiting for over 30 years!**

*Led by Professors Olivier Rascol, a neuropharmacologist at Toulouse University Hospital, and Wassilios Meissner, a neurologist at Bordeaux University Hospital, both members of NS-PARK\* (F-CRIN\*\*), the French clinical research network on Parkinson's disease behind the project, the LixiPark study is the first multicentre clinical trial to show that lixisenatide, a drug already developed and marketed for the treatment of type 2 diabetes, may slow the progression of motor symptoms in Parkinson's disease. This represents a world first in this field, **and has just been published in the prestigious New England Journal of Medicine!***



Parkinson's disease is a neurodegenerative disorder affecting 250,000 people in France and 10 million worldwide. It is a gradual process that worsens over time, mainly leading to motor disorders (slowness of movement, stiffness of the limbs, tremor), and causing disability and loss of independence for many patients. The motor symptoms of this disease result from the progressive disappearance in the brain of the dopaminergic neurons responsible for producing dopamine, the chemical molecule that plays a role in controlling movement. For the last 50 years, drugs such as L-DOPA have been available to correct the lack of dopamine, thereby mitigating the clinical expression of symptoms. However, they are ineffective in halting the worsening of symptoms over the years because they do not tackle the cause of the disease (the progressive loss of dopaminergic neurons) but rather its consequence (the lack of dopamine). Preliminary data in models of Parkinson's disease suggested that drugs already used to treat diabetes, such as GLP-1 receptor agonists (the class that includes lixisenatide), may improve the survival of dopaminergic cells and could therefore slow the progression of Parkinson's disease. The effects on patients had yet to be assessed.

The LixiPark clinical trial therefore studied the potential benefits of this drug in patients with Parkinson's disease. The first test phase is now coming to an end, and its positive results send a message of hope to sufferers.

For one year, teams from 21 research centres in the French NS-PARK\* network conducted a double-blind, placebo-controlled trial to assess the efficacy of lixisenatide in 156 volunteer patients aged between 40 and 76 at the start of disease progression. Their results confirmed the initial hypothesis: after one year of follow-up, the overall motor symptom score of the placebo group worsened by three points, whereas the score of the lixisenatide-treated group remained unchanged, with no sign of aggravation. This difference was significant, and the most plausible interpretation of this observation is that the loss of dopaminergic neurons was lower in patients given lixisenatide than in those given the placebo, indicating that the drug had a "neuroprotective" effect.

*"For 30 years, we have been trying to understand how to slow the decline associated with Parkinson's disease. Numerous researchers have attempted to find answers, but have been unsuccessful so far in patients. In the LixiPark study, we began with the premise that diabetic subjects seem to have an increased risk of developing Parkinson's disease, and that it seems to progress more rapidly in them. At the same time, laboratory tests have provided evidence that receptors involved in the mechanisms of diabetes may also play a role in the mechanisms responsible for the loss of certain neurons in the brain. Since drugs such as lixisenatide were already available to treat diabetes, we decided to assess their effects in patients with Parkinson's disease. As we had hoped, the results we obtained supported a neuroprotective effect. This is the first large-scale, multicentre clinical trial to provide the signs of efficacy that have been sought for so many years. It is a truly innovative result, as we currently only have 'symptomatic' antiparkinsonian treatments, which mask clinical expression of signs of the disease but are ineffective in preventing its cause and its worsening over time. These initial positive results showing slower progression of Parkinson's disease therefore constitute a significant step forward in the future management of this disease and are of major importance to public health,"* commented Professors Olivier Rascol and Wassilios Meissner.

Both also stressed that the LixiPark study is only the first stage in a long process before "routine" treatment of Parkinson's sufferers with drugs such as lixisenatide can be considered. Further studies will be needed to confirm the drug's efficacy and safety for this potential indication, and to better assess the risk-benefit ratio in patients at different stages of the disease who are followed up for more than a year.

### **A study supported by numerous public and private players**

A phase 2 trial coordinated by Professors Olivier Rascol (NS-PARK, F-CRIN, Toulouse University Hospital and University of Toulouse) and Wassilios Meissner (NS-PARK, F-CRIN, Bordeaux University Hospital and University of Bordeaux), LixiPark was made possible by the support and contribution of numerous public and private players: Toulouse University Hospital, the study's sponsor; the Toulouse Clinical Investigation Centre, which coordinated its implementation; F-CRIN, the French clinical research infrastructure network supported by Inserm, through two of its 20 components (the NS-PARK network, which designed the trial and recruited the patients, and the Euclid platform, which analysed the results); the French Ministry of Labour, Health and Solidarity, which funded part of the project (PHRC-16-0402); Cure Parkinson, an English charitable foundation, which funded the other part of the study; and the pharmaceutical company Sanofi, which provided the drug and placebo free of charge.

#### **\* About NS-PARK (F-CRIN)**

The NS-PARK network (F-CRIN), which received F-CRIN accreditation in 2014, is a national clinical research network specialising in Parkinson's disease and movement disorders. It brings together investigators and clinical researchers from 27 French centres, including the 25 Parkinson's expert centres in France. It is governed by an executive board consisting of a coordinator, Professor Olivier Rascol (Toulouse), a co-coordinator, Professor Jean-Christophe Corvol (Paris, Pitié Salpêtrière), and associates Professor David Devos (Lille) and Professor Stéphane Thobois (Lyon). NS-PARK's goal is to facilitate clinical research into Parkinson's disease and movement disorders and contribute to the development of innovative

therapies to improve the care of patients suffering from these diseases. The network is accredited and funded by the F-CRIN national clinical research infrastructure. It also receives annual financial support from Inserm and the Ministry of Health as part of the Neurodegenerative Diseases Plan (MND Plan) of the General Directorate for Healthcare Services (DGOS).

**\*\* About F-CRIN**

Created in 2012, supported by Inserm and funded by the French National Research Agency (ANR) and the Ministry of Health, the French Clinical Research Infrastructure Network (F-CRIN) is an infrastructure of excellence supporting clinical research in France. Its aim is to boost the international competitiveness of French clinical research, identify and accredit research networks, facilitate the implementation of academic or industrial clinical trials, and develop the expertise of clinical research players, by pooling know-how, goals and resources. The organisation, whose national coordination unit is based in Toulouse, has accredited and brought together 16 clinical investigation networks targeting diseases of importance to health (Motor neurone disease/Charcot's disease, Sepsis, Autoimmune and autoinflammatory diseases, Severe asthma, Cardiovascular diseases, Multiple sclerosis, Obesity, Psychotic disorders, Atopic dermatitis, Retinal diseases, Cardio-renal diseases, Thrombosis, Vaccinology, Parkinson's disease and movement disorders, Paediatrics, Stroke), as well as three expertise and methodology networks (Rare diseases, Medical devices, Epidemiology) and a platform for customised support offering all the services needed to conduct clinical trials. In total, F-CRIN brings together a community of over 1400 clinical research professionals. It receives support from Inserm, the French Ministry of Health, several university hospitals, universities, foundations and industry. For more information: <https://www.fcrin.org/en>

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