1	Sponsor: CHRU de Lille Direction de la Recherche et de l'Innovation, 2 avenue Oscar Lambret, 59037 LILLE Cedex FRANCE
2	Name of investigational medicinal product: Deferiprone
3	Name of active substance(s): Deferiprone
4	Full title of research: Conservative iron chelation as a disease-modifying strategy in Parkinson's disease. It's a European multicenter, parallel-group, placebo-controlled, randomized clinical trial of deferiprone (DFP) - FAIRPARKII
5	Investigator(s)[1] : Coordinating investigator: Prof. David DEVOS

Country	Sites	Principal Investigator	Number of co-investigators by site
France	Lille	Pr Defebvre Luc	3
	Toulouse	Pr Rascol Olivier	7
	Strasbourg	Pr Tranchant Christine	2
	Marseille	Dr Eusebio Alexandre	4
	Lyon	Pr Thobois Stéphane	4
	APHP (Paris)	Pr Corvol Jean-Christophe	7
	Clermont-Ferrand	Pr Durif Franck	3
	Bordeaux	Pr Meissner Wassilos	4
Spain	Hospital Clinic in Barcelona	Dr Yaroslau Compta	1
	Germans Trias I Pujol Hospital	Dr Dolores Vilas	2
	Hospital Sant Pau	Dr Jaime Kulisevsky	2
Austria	Medizinische Universitat Innsbruck	Pr Werner Poewe	9
Czech Republic	Univerzita Karlova V Praze	Pr Evzen Ruzicka	2
UK	Cambridge	Dr Paul Worth	1
	Newcastle	Pr Nicola Pavese	3
Portugal	Centro Hospitalar do Alto Ave	Dr Miguel Gago	1
	Centro Hospitalar e Universitario de Coimbra	Dr Cristina Januario	2
	Centro Hospitalar Lisboa Norte	Pr Miguel Vilhena Soares Coelho	6
Germany	Christian-albrechts-universität zu kiel	Pr Daniela Berg	3
	Homburg	Dr Stefanie Behnke	3
	Rostock	Dr Uwe Walter	1
Netherlands	Radboudumc	Dr Bart Post	5
	Academic Central Center	Pr Rob de Bie	1

Total number of investigators : 99

[1] Si la recherche est multicentrique, indiquer le ou les noms des investigateurs coordonnateurs et le nombre total d'investigateurs.

6 Research sites and centers[2]:
Total number of centers: 23

Country	Sites
France	Lille
	Toulouse
	Strasbourg
	Marseille
	Lyon
	APHP (Paris)
	Clermont-Ferrand
	Bordeaux
Spain	Hospital Clinic in Barcelona
	Germans Trias I Pujol Hospital
	Hospital Sant Pau
Austria	Medizinische Universitat Innsbruck
Czech Republic	Univerzita Karlova V Praze
UK	Cambridge
	Newcastle
Portugal	Centro Hospitalar do Alto Ave
	Centro Hospitalar e Universitario de Coimbra
	Centro Hospitalar Lisboa Norte
Germany	Christian-albrechts-universität zu kiel
	Homburg
	Rostock
Netherlands	Radboudumc
	Academic Central Center

7 Publications[3] : **Trial of deferiprone in Parkinson's disease**
Publication accepted in the New England Journal of Medicine with reference: **N Engl J Med 2022;387:2045-55. DOI: 10.1056/NEJMoa2209254**

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[2] Indiquer le nombre de lieu(x) de recherches et de centres (s'il diffère du nombre de lieux).
[3] Préciser dans l'ordre : le nom des auteurs, le titre de la publication, le nom de la revue, l'année, le numéro du tome, les pages concernées.

	5 CHU Lille, Direction de la Recherche et de l'Innovation, F-59000 Lille, France 6 Department of Neurology, Medical University Innsbruck, Austria 7 Parkinson's Disease & Movement Disorders Unit, Hospital Clínic de Barcelona / IDIBAPS / CIBERNED (CB06/05/0018-ISCIII) / European Reference Network for Rare Neurological Diseases (ERN-RND), Maria de Maeztu excellence center - Institut de Neurociències, Universitat de Barcelona, Catalonia, Spain 8 Clinical Ageing Research Unit, Newcastle University, Newcastle upon Tyne, UK 9 Department of Neurology and Center of Clinical Neuroscience. First Faculty of Medicine, Charles University and General University Hospital, Prague, Czechia 10 Radboud University Medical Center; Donders Institute for Brain, Cognition and Behaviour; Dept. of Neurology; Nijmegen, The Netherlands 11 Department of Neurology. Christian-Albrechts-University Kiel, Germany 12 Department of Neurology. University clinic, Ulm. 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8 8.1 8.2	Duration of research: - date of first inclusion: 09/02/2016 - date of end of participation of the last person included in the research: 22/09/2020
	9. Clinical trial phase: IIb
10	Primary and secondary research objectives: Objective 1: To successfully manage the demonstration of the Investigating DFP efficacy as a treatment for PD in a large placebo-controlled study and thus demonstrate (for the first time in a neurodegenerative disease) the concept of conservative iron chelation as a disease modifier treatment. We aim to demonstrate a lower progression of motor and non-motor handicap at week 36 in PD receiving DFP as compared with placebo. Objective 2: To demonstrate the feasibility of a multi-site European clinical trial of a potential PD treatment with a demonstrated safety profile, with a specific monitoring. Objective 3: To fund the larger scale investigation of DFP in PD patients, which the existing

	preclinical and clinical data strongly mandate and to promote a European clinical trial network of PD clinicians and researchers. Objective 4: To investigate clinical, radiological, biological and genetic biomarkers of PD progression in response to DFP. Objective 5: To bring the first data of DFP's potential real-world benefits based upon the drug's impact on health economics aspects and the continuous monitoring of motor and non-motor handicap at home. Objective 6: To expedite the availability of disease-modifying treatments to PD patients. Based upon our demonstration of efficacy and safety of conservative iron chelation with the only available and prototype drug, DFP, we aim to promote and support the clinical development of iron chelators as a new treatment modality in PD. The following clinical development with large phase II studies and registration of DFP, the first in class, by ApoPharma could be done within 7 years. We also aim to promote the clinical development (from phase I) of future other iron chelators (i.e. hydroxypyridinones) for PD and other neurodegenerative diseases (i.e. Alzheimer, ALS, multisystem atrophy, etc.). Objective 7: To describe the effect of DFP on the disease progression, taking into account the dropout rate with a combined criterion of disease progression measured by the total score of the MDS-UPDRS and the dropout because of disease worsening.
11	Research methodology [4] : A multicentre, parallel-group, randomized, placebo-controlled trial of DFP 15 mg/kg BID. A 9-month treatment period (period 1) will be followed by a 1-month post-treatment monitoring period (period 2), in order to assess the disease-modifying effect in the absence of a symptomatic effect (i.e. an effect of inhibition of catechol-O-methyl transferase (COMT) activity (ICOMT) on dopamine metabolism) of DFP (versus placebo). Considering the short half-life of DFP, one month will be enough to assess the level of handicap of patients in the absence of ICOMT due to DFP treatment. **Description of the procedures performed:** Screening visit: The screening will include the following: - Medical History and Clinical Examination - Mini Mental State Examination - Demography and disease history - Concomitant Medications - Medications taken during the past 3 months - Weight, height, Electrocardiogram - Columbia Suicide Severity Rating Scale - Checklist of inclusion and exclusion criteria - Laboratory test: o Blood count, haemoglobin, haematocrit, o Hepatic (ASAT, ALAT, alkaline phosphatase, bilirubin, gamma GT), o Hepatic tests (B and C) o Kidney tests (ionogramm and urea creatinine) o Iron status (ferritin, serum iron, transferrin, transferrin saturation coefficient, Serum Total Iron-Binding Capacity) o Other metals (copper, zinc) o β HCG (for non-menopausal women) o Hormonal status (FSH-LH) for women o Fasting glucose - Patients have to bring back the 24h urine sample for the randomization visit Randomization visit: The randomization visit will include the following: - Clinical Examination - Weight, Electrocardiogram, - Eligibility Screening, Checklist of inclusion and exclusion criteria

[4] Préciser notamment si la recherche comporte un tirage au sort, si elle est comparative, en ouvert, en simple insu, en double insu, à groupes parallèles, en plan croisé, les types de comparateurs utilisés.

- Randomization by IWRS system
- Minimal Specific biochemistry with 24-hour urine iron (samples for central analysis)
- Total MDS- UPDRS
- MOCA
- Stand Walk Sit test
- PDQ-39: quality of life
- Health economics questionnaire
- EQ-5D
- Adverse event and serious adverse event
- Optional studies and ancillary studies
    - Specific biochemistry *(150<n<338) (samples for central analysis)
    - Additional blood analyses (lymphocytes and microparticles) (samples for central analysis)
    - Lumbar puncture (samples for central analysis) and coagulation assessment
    - Transcranial ultrasound
    - SENSEPARK
    - DatScan
    - MRI
- β HCG (for women of childbearing potential)

A weekly CBC (with the WBC) for the first 24 weeks and then monthly until week 36. The results will be immediately faxed by the patient's local medical lab or the study center's central lab.

Visit 1: Week 12 and Visit 2: Week 24:
The visit 1 will include the following:
- Clinical Examination
- Weight, Electrocardiogram,
- Concomitant treatment
- Clinical and Patient Global Impression
- Total MDS- UPDRS
- Columbia Suicide Severity Rating Scale
- Laboratory test
    - Blood count, haemoglobin, haematocrit,
    - Hepatic (ASAT, ALAT, alkaline phosphatase, bilirubin, gamma GT),
    - Kidney tests (ionogramm and urea, creatinine)
    - β HCG (for non-menopausal women)
    - fasting glucose
- Adverse event and serious adverse event
- Treatment compliance
- CBC (with the WBC)

Visit 3: Week 36:
The visit 3 will include the following:
- Clinical Examination
- Weight, Electrocardiogram
- Concomitant treatment
- Minimal Specific biochemistry (samples for central analysis)
- Laboratory test
    - Iron status (ferritin, serum iron, transferrin, transferrin saturation coefficient, 24-hour urine iron, Serum Total Iron-Binding Capacity)
    - Other metals (copper, zinc)
    - β HCG (for women of childbearing potential)
- Treatment compliance
- Total MDS- UPDRS
- Columbia Suicide Severity Rating Scale
- MOCA
- Stand Walk Sit test
- PDQ-39: quality of life
- Clinical and Patient Global Impression

	- Health economics questionnaire - EQ-5D - Adverse event and serious adverse event - Optional studies and ancillary studies o Specific biochemistry *(150<n<338) (samples for central analysis) o Additional blood analyses (lymphocytes and microparticles) (samples for central analysis) o Lumbar puncture (samples for central analysis) and coagulation assessment o Transcranial ultrasound o SENSEPARK o MRI <u>Visit 4: Week 40:</u> The visit 4 will include the following: - Clinical Examination - Weight, Electrocardiogram - Total MDS- UPDRS - MOCA - Stand Walk Sit test - PDQ-39: quality of life - Clinical and Patient Global Impression - event and serious adverse event - Ancillary studies o SENSEPARK o DatScan - β HCG (for women of childbearing potential) A phone call for safety will be performed every month by the medical team
12 12.1 12.2	Number of people who took part in the research: - number of people planned: 372 - number of people analyzed: 372 for Intention-to-treat analysis and 160 for Per-protocole analysis.
13	Medical condition or pathology studied and main inclusion and non-inclusion criteria: <u>Parkinson's disease in de novo patients.</u> <u>Inclusion criteria:</u> 1. Adult Patients 2. Parkinson's disease diagnosed according The Movement Disorder Society Clinical Criteria for Parkinson's Disease (PD) 3. Treatment-naïve, i.e. the best population for assessing a disease-modifying effect without the interaction of dopaminergic treatment (no dopaminergic agonists, L-dopa, anticholinergics, monoamine oxidase B inhibitors (e.g. rasagiline) or deep brain stimulation). 4. Patients covered by a Health Insurance System in countries where required by law 5. Written informed consent dated and signed prior to the beginning of any procedures related to the clinical trial <u>Exclusion criteria:</u> 1. Disease duration greater than 18 months. 2. Patients with high frequency of comorbidity or vital risks that may reasonably impair life expectancy 3. Subject with handicap required dopaminergic treatment at the inclusion and therefore likely not to bear 9 months without symptomatic treatment 4. Hoehn and Yahr stage 3 or more. 5. Significant cognitive impairment (a Mini Mental State Examination score <24 or an equivalent impairment on a similar scale) or dementia diagnosed in accordance with the Movement Disorders Society criteria (Emre et al., 2007).

	6. Atypical or secondary parkinsonism (supranuclear palsy, multisystem atrophy, etc.) or significant cortical or subcortical atrophy (i.e. atypical for PD). 7. Progressing axis I psychiatric disorders (psychosis, hallucinations, substance addiction, bipolar disorder, or severe depression), in accordance with the Diagnostic and Statistical Manual of Mental Disorders. 8. Subjects undergoing brain stimulation. 9. Due to the high risk of agranulocytosis caused by the IMP and the unknown mechanism by which this agranulocytosis is induced, it is not allowed to combine Deferiprone with other medicinal products causing agranulocytosis (as described in the IB). Such medicinal products are the already mentioned clozapine and also some NSAIDs (e.g. Phenylbutazone or Metamizole), antithyroid agents, sulfonamide antibiotics or metothrexate. 10. A history of relapsing neutropenia 11. Hypersensitivity to deferiprone. 12. Patients with agranulocytosis or with a history of agranulocytosis. 13. Patients taking a treatment at risk of agranulocytosis (clozapine, Closaril®/Leponex®). 14. Patients with anaemia (regardless of the latter's aetiology) or a history of another haematological disease. Haemochromatosis is not an exclusion criterion. 15. Pregnant or breastfeeding women or women of childbearing potential not taking highly effective contraception. 16. Kidney or liver failure. 17. Other serious diseases. 18. Inability to provide informed consent. 19. Participation in another clinical trial with investigational medicinal product within 3 months prior to inclusion in the study 20. Patient who has suffered mild or moderate depressive episode and isn't in remission and on a stable medication for at least 8 weeks 21. Patient > 130kg
14	Investigational medicinal product studied[5] (name, dose, route of administration and batch numbers): DEFERIPRONE, 30mg/kg/day, oral, Batch number P003142, P002617, P003686, P005781
15	Treatment duration[6] : 9 months
16	Reference investigational drug(s)[7] (name, dose, route of administration and batch numbers), if applicable: Not applicable
17	Evaluation criteria:
17.1	- efficacity: **The primary efficacy criterion**: the change in the total MDS-UPDRS score between baseline and 36 weeks (i.e. the end of the placebo-controlled phase for analysis of both disease-modifying and symptomatic effects). Experience from the large ADAGIO and ELLDOPA studies indicates that we shall be able to maintain de novo PD patients in the absence of symptomatic treatment for 36 weeks with a low drop-out rate - a sufficiently long time period over which to observe a difference vs. the placebo group). The total MDS-UPDRS score is the usual primary efficacy criterion in PD trials. It includes all the motor and non-motor aspects of the disease and the activity of daily living (part II), which is less sensitive to the placebo effect.
17.2	- security: - A weekly complete blood count (with differential leucocytes count and absolute neutrophils count) will be performed weekly (± 3 days) from the start of treatment onwards for 24 weeks and then monthly until week 36. For the patients' comfort, the test can be performed in a

[5] Répéter la section si la recherche porte sur plusieurs médicaments expérimentaux étudiés.
[6] Préciser, le cas échéant, pour chaque médicament expérimental étudié, la durée maximale de traitement pour la personne qui s'est prêtée à la recherche.
[7] Répéter la section si la recherche comporte plusieurs médicaments expérimentaux de référence.

	medical laboratory close to their home. The results will be immediately faxed to the study centre. A standard operating procedure (SOP) in each centre will ensure prompt review of the results. An additional WBC count will be required in the event of fever. If the ANC falls below a value of 1.5 x 10^9/L (neutropenia) and/or 0.5 x 10^9/L (agranulocytosis), the investigator will immediately contact the patient and take appropriate measures. Therapeutic education and SOP in case of fever, neutropenia or agranulocytosis will be also provided to all the patients - An iron status check: haemoglobin, serum iron, ferritinemia, transferrin, total binding capacity, transferrin saturation coefficient, 24-hour urine iron. - Clinical chemistry tests: fasting glucose, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT). Contraceptive counselling will also be provided for all sexually active males and females). - General health status and a full physical examination, including vital signs, bodyweight, electrocardiogram and blood pressure. - Adverse events, concomitant medication(s) and observance: participants will be questioned about the occurrence of AEs, the use of any medications and the compliance with the study therapy, at each scheduled or unscheduled visit. - β HCG (for women of childbearing potential) will be performed every month and the result will be immediately faxed by the patient's local medical lab
17.3	<u>- others :</u> (i) The disease-modifying effect: will be measured as the changes in the overall MDS-UPDRS score between baseline and week 40 (i.e. the end of the one-month post-treatment monitoring period), to analyse the disease-modifying effect without bias from the symptomatic effect of ongoing DFP treatment) on the study population as a whole (n= 372). (ii) The global effect on motor and non-motor symptoms: will be analysed as the change in the different subscales of the MDS-UPDRS (part I: cognition and behaviour; part II: activities of daily living; part III: motor handicap; part IV: fluctuations) and MDS-UPDRS part II+III, the Stand Walk Sit test, overall cognitive status (score in the Montreal Cognitive Assessment) between baseline and week 36; and between baseline and week 40 for the study population as a whole (n= 372). (iii) Effects on quality of life and autonomy will be analyzed as the change in the Parkinson's Disease Quality of Life (PDQ-39, via a 39-item self-questionnaire) and the Clinical Global Impression scored by the examiner and the patient between baseline and week 36, and between baseline and week 40 for the study population as a whole (n= 372). (iv) A health economics assessment will be performed via a specific questionnaire and EQ-5D questionnaire (It provides a simple descriptive profile and a single index value for health status) between baseline and week 36 on the study population as a whole (n= 372).
18	Statistical analysis: See attached PDF document « SAP-FP II V.finale »
19	Summary - research findings
19.1	***- Results of effectiveness evaluation, if applicable:*** We randomized 372 patients to receive deferiprone (n=186) or placebo (n=186). The total MDS-UPDRS score increased by 15.6 points in deferiprone-treated patients and by 6.3 points for patients treated with placebo (mean difference, 9.3 points; 95% CI, 6.3 to 12.2; P<0.0001). Nigro-striatal iron content was reduced in the deferiprone-treated group versus placebo.
19.2	***- Results of safety assessment, if applicable:*** The main serious adverse events under deferiprone included agranulocytosis in 2 patients and neutropenia in 3 patients.
19.3	***- Conclusion***: This 36-week phase 2, randomized, placebocontrolled trial showed that deferiprone did not slow the progression of Parkinson's disease in participants who had never received levodopa. To the

contrary, deferiprone was associated with worsening of motor and nonmotor symptoms over a period of 36 weeks. Neuroimaging findings in a subgroup of participants showed target engagement of deferiprone with a greater reduction of iron content in nigrostriatal pathways, and particularly in the substantia nigras, than with placebo. These findings were paradoxically associated with decreased basal ganglia volume in the placebo group and increased volume in the deferiprone group and a lack of betweengroup differences on DaT imaging.
The apparent detrimental clinical effects of deferiprone on symptoms of Parkinson's disease became evident as more participants in the deferiprone group than in the placebo group discontinued the trial agent and wished to start dopaminergic therapy owing to disease progression, and by the visual inspection of graphs of MDS-UPDRS scores at the first scheduled visit at month 3, but no formal analysis of this time course was carried out. We speculate that the early separation of curves in favor of the placebo group may be consistent with a negative symptomatic effect of deferiprone rather than an accelerating effect on underlying disease progression. This conjecture is based on chelation of brain iron by deferiprone that presumably reduced activity of tyrosine hydroxylase, the ratelimiting enzyme for dopamine production, which is consistent with the increased levels of plasma prolactin, an inhibitor of which is dopamine. Had there been a reduction in the difference in outcomes between the two trial groups after discontinuation of deferiprone between weeks 36 and 40, a putative negative symptomatic effect would have been supported, but this was not observed, possibly because it takes more than 4 weeks to recharge the nigrostriatal pathway with iron as a compensatory mechanism to ensure dopamine synthesis.
Hematologic risks of deferiprone at the low doses used in the trial were evident in 5% or fewer of the participants. Normal iron levels in red cells (i.e., mild reduction of the iron-storage marker ferritin without anemia) and iron levels that were reduced only in the nigro-striatal pathway showed conservation of systemic iron despite chelation.
This trial has limitations. The results and their interpretation should be viewed in the context of our hypothesis that deferiprone would be superior to placebo in clinical outcomes, and we found the opposite. There was also a need for imputation of a large amount of clinical outcome data owing to participant dropout, particularly in the deferiprone group, and a lack of racial diversity. Whether participants receiving dopaminergic therapy would have a different outcome remains unclear, but in trials of deferiprone involving a total of approximately 240 participants who were receiving dopaminergic therapy, no worsening in scores of Parkinson's disease activity was observed with this agent, and some participants even had improvement in such scores.
Despite evidence of target engagement of iron reduction in the substantia nigra of participants with Parkinson's disease who had never received levodopa and in whom treatment with a dopamine agonist was not planned, deferiprone was not associated with benefit as compared with placebo in measures of the progression of Parkinson's disease, and there was evidence of clinical worsening.

ClinicalTrials.gov (NCT02655315)

Summary for the general public:
Parkinson's disease (PD) affects over 6 million people worldwide. It is characterized by the loss of brain cells (neurons) that produce dopamine - a neurotransmitter essential for controlling movement. Drug treatments that replace dopamine improve symptoms but do not slow the loss of nerve cells or the progressive worsening of the disease.

Iron accumulates in the brains of people with PD and excessive levels of iron have been implicated in the loss of dopamine-producing neurons. It has been shown in experimental models that reducing excess iron with chelating drugs prevents its toxic effects and limits this neuronal death. However, iron is also important for the proper functioning of many biological processes, including the production of dopamine itself. Iron can therefore have both beneficial

and detrimental effects.

Deferiprone is an iron chelator that has the ability to remove iron from overloaded areas while redistributing it to areas that need it. It has been used to treat iron overload in a rare red blood cell disease (called "thalassemia") for many years. Two earlier clinical trials in a small number of Parkinson's patients suggested that treatment with deferiprone given in addition to the usual dopamine replacement drugs, such as L-DOPA, reduced the accumulation of iron in the brain and improved motor disability.

The objective of the European multicenter FAIRPARK-II study was to investigate the effect of deferiprone on the progression of PD. The study, funded by the European H2020 program, promoted by the Lille University Hospital, was coordinated by Prof. Devos with the strategic support of the NS-PARK network, which brings together all the French expert centers on Parkinson's disease accredited by the National Clinical Research Infrastructure F-CRIN, the European Clinical Research Organization ECRIN, and Inserm Transfer. Its results have just been published in the New England Journal of Medicine.

The FAIRPARK-II study enrolled 372 people with PD at 23 European centers to determine whether deferiprone could slow disease progression when given at the very beginning of the disease, before dopamine replacement drugs are started, at a stage when more dopaminergic neurons remain.

People in the study received either oral deferiprone (30 mg/kg/day) or placebo for 9 months. Patients and physicians were blinded to the treatments administered throughout the study.

Analysis of the results showed that deferiprone reduced iron levels in areas of the brain important for movement control. Using the standard clinical assessment scales for PD, there was a deterioration in movement and quality of life in patients taking placebo over the 9 months. Surprisingly, and contrary to the study hypothesis, those treated with deferiprone experienced a small but significant greater deterioration than the placebo group over the 9 months. In contrast, markers of dopamine neuron loss were not different between the two groups, showing that deferiprone did not precipitate neuron loss, but likely had a deleterious effect on motor symptoms without altering neuron loss.
These results are in stark contrast to the other 4 independent trials involving about 240 people with PD, where no worsening of symptoms was observed. The major difference between these trials and the FAIRPARK study is that in the other 4 studies all participants were already receiving dopamine replacement drugs, such as L-DOPA, in addition to deferiprone. This is probably where the explanation for these conflicting results lies.

By the time a person is diagnosed with PD, they have already lost about 50% of the dopamine-producing neurons in their brain. The remaining neurons must therefore be more active to maintain dopamine production and facilitate movement. As mentioned above, iron facilitates dopamine synthesis by serving as an important cofactor for the key enzyme, tyrosine hydroxylase, which catalyzes the first step in dopamine synthesis. Therefore, in the early stages of PD, iron accumulation may help neurons compensate for dopamine synthesis even though, over time, iron accumulation becomes toxic. Iron removal in the early stages may therefore be at the expense of dopamine synthesis, resulting in a slight deterioration in movement control in patients taking deferiprone, but without accentuating neuronal loss. On the contrary, previous trials have shown that deferiprone could slow it down. In these trials, the effects of deferiprone on dopamine synthesis were offset by treatment with L-DOPA, the precursor of dopamine, and it therefore had no deleterious effect on symptoms.

	The FAIRPARK II study has led to a better understanding of the complex role of iron in Parkinson's disease: a positive role in compensatory phenomena by increasing dopamine synthesis at the very beginning of the disease, and a deleterious role, accelerating neuronal loss due to its accumulation at later stages. The possibility of its elimination by iron chelators such as deferiprone has therefore not been abandoned, quite the contrary! However, in the future, its efficacy will have to be tested in conjunction with dopaminergic treatment (with L-DOPA) in Parkinson's disease. Deferiprone is also currently being tested in other neurodegenerative diseases such as amyotrophic lateral sclerosis, parkinsonian syndromes or Alzheimer's disease. We are therefore continuing our research because neuroprotective treatments are one of the greatest needs of people suffering from Parkinson's disease or any other neurodegenerative disease.
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