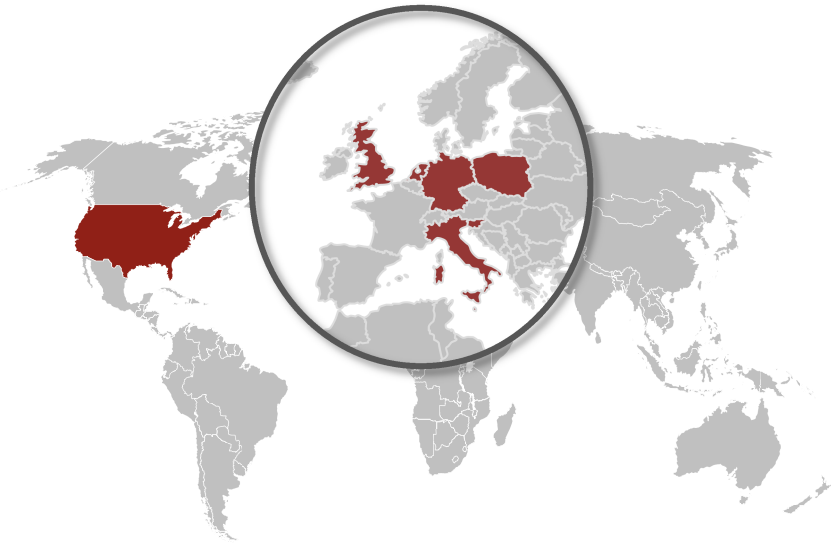
TIRCON

Treat **I**ron-**R**elated **C**hildhood-**O**nset **N**eurodegeneration



TIRCON Clinical Study

A Deferiprone-trial in patients with Pantothenate Kinase-Associated Neurodegeneration (PKAN)

Information leaflet

FP7 (277984-2)

SEVENTH FRAMEWORK PROGRAMME

What is the study about?

The study refers to **Pantothenate Kinase-Associated Neurodegeneration (PKAN)**, a form of **Neurodegeneration with Brain Iron Accumulation (NBIA)**, caused by alterations in the PANK2-gene. PKAN accounts for about 50 % of all NBIA cases. As it can be relentlessly progressive, seriously disabling and life-threatening, there is an urgent and so far unmet need for causative therapies with the potential to halt or even reverse the course of the disease.
PKAN is characterized by abnormally high iron levels in the basal ganglia. It is not completely understood why the brain iron levels in NBIA-patients are high, but it is presumed to have harmful effects.
The purpose of this clinical trial is to investigate if the iron-chelating drug **Deferiprone** can remove brain iron by oral (taken by mouth) medication. Clinical examinations during the study shall explore if Deferiprone has an impact on the course of the disease.
The drug will be tested for 18 months in 90 patients. The study will be carried out at five centers: Munich (Germany), Warsaw (Poland), Milan (Italy), Newcastle (United Kingdom) and Oakland (California in the United States).

What kind of study is it?

This study is **a randomized, double-blind, placebo-controlled trial**.
"Placebo-controlled" means that in the context of this study, Deferiprone will be compared with a placebo. A placebo looks identical to the Deferiprone but does not contain any active ingredient. The study participants will have a two in three chance of getting Deferiprone and a one in three chance of getting the placebo. The selection will be done by randomization.
"Randomization" is done according to a computer generated randomization list. Every patient would be allocated to either placebo or Deferiprone group according to this list. It is necessary to compare the drug with a placebo group to fully assess the effects and side effects of Deferiprone.
"Double-blinding" means that neither the patient nor the physicians know in which group the patient will be included. This is necessary for an objective collection of study data.

Who can take part in the study?

The study participants will be ages 4 to adult and must have PKAN disease, confirmed by genetic testing.
For other inclusion/exclusion criteria, please contact the study center next to you.

What will happen in the study?

Medication:
The study participants will take Deferiprone or the placebo for 18 months in a daily dose, always divided into two parts, half given in the morning and half given at night. The patients will be started with a dose of 10 mg per kilogram daily. If there are no problems the dose will be increased to 20 mg after six weeks and 30 mg after twelve weeks for the rest of the study.

Tests:
For taking part in this study, the following tests have to be completed:

What?	*Where?*	*When?*
Screening Visit (interview, physical examination, blood and urine sample, evaluation of dystonia and ECG for suitability testing, …)	TIRCON clinical center	prior to the study
Baseline Visit (complete physical exam, a blood and urine sample, medical history, MRI[1], evaluation of dystonia, mobility, cognition, quality of life and sleep, motor functions and emotional condition, video recording, administration of Deferiprone)	TIRCON clinical center	at the beginning of the study
Telephone contacts	-	week 1, 2, 3, 4, and 5
Blood samples for white blood cell counts (Each weekly visit will take about 30 minutes.)	local doctor's office or lab	weekly (every 5-10 days)
Visit (interview, physical exam, blood and urine sample…)	TIRCON clinical center or local doctor's office	month 1.5
Telephone contact	-	month 2
Visit (interview, physical exam, blood and urine sample…)	TIRCON clinical center or local doctor's office	month 3
Visits (similar to the baseline visit)	TIRCON clinical center	month 6 and 12
Telephone contacts	-	month 9 and 15

[1] Patients with Deep Brain Stimulation (DBS) will be excluded from MRI examinations.

Visit for final testing (similar to the baseline visit)	TIRCON clinical center	month 18
Visit for final check up (including an interview and blood sample)	TIRCON clinical center	month 19, after the ending of the study

Reimbursement and Costs:
Study participants will not be paid for being in this study. Their travel expenses will, however, be covered.

What are the benefits of being in the study?

There is no guarantee that patients will get any benefit from this study. However, the participations in this study are needed to better understand the effectiveness of the drug Deferiprone.
It is expected that study patients who use Deferiprone as directed will have a reduction in the amount of iron in the brain. This might result in an improvement of NBIA symptoms like dystonia and of quality of life and skills.
If the trial results prove to be positive, Apopharma will offer Deferiprone on a compassionate-use basis at no cost to all study participants.

What are the risks of being in the study?

Deferiprone is an investigational drug. Information on the safety of Deferiprone has been collected from over 1000 patients, but only few of them had NBIA. Possible side effects could be:

- reddish discoloration of the urine
- nausea / vomiting
- joint pain
- abdominal pain
- increase in ALT (an enzyme in the liver that measures liver function)
- neutropenia / agranulocytosis (a lowered white blood cell count)
- allergic reactions
- other unexpected reactions

Who can I contact with further questions?

More detailed information about the study will be available at the study center next to you:

http://tircon.eu/nbia-clinical-network/tircon-clinical-centres