DEEP - DEferiprone Evaluation in Paediatrics

DEEP-2

Mission completed!

Efficacy of deferiprone versus deferasirox in paediatric patients affected by hereditary haemoglobinopathies

Lay summary

Thank you!

Clinical study participants are part of a large international community that helps researchers to find important answers to health questions and to discover new medical treatments.
So, your help has been pivotal in the DEEP-2 clinical study, and we would like to thank you for taking part in it.

The scope of this booklet is to provide a summary of DEEP-2 clinical study explaining its objectives and its achieved results.

What was the DEEP-2 study about?

DEEP-2 clinical trial aimed to demonstrate the efficacy and safety in children affected by hereditary haemoglobinopathies of deferiprone, a medicine already used in adults and older children. The study was part of the DEEP project (short for DEferiprone Evaluation in Paediatrics, in other words find out how deferiprone works in kids).

Clinical Trial Identification

TITLE OF THE STUDY
Multicentre, randomised, open label, non-inferiority active-controlled trial to evaluate the efficacy and safety of deferiprone compared to deferasirox in paediatric patients aged from 1 month to less than 18 years affected by transfusion dependent haemoglobinopathies.

ACRONYM/ BRIEF TITLE DEEP-2

EUdraCT NUMBER* 2012-000353-31

PRODUCT Deferiprone

DATE OF THIS SUMMARY
30 June 2022

*EudraCT Number is an identification number assigned to each trial by the European Union Drug Regulating Authorities Clinical Trials Database (EudraCT), a collection of clinical trials on medicines authorized in the European Union.

Why was the DEEP-2 study needed?

Hereditary haemoglobinopathies are a large family of genetic diseases which affect the blood, such as thalassemia or sickle cell anaemia. They have different symptoms and manifestations but share a common effect: they make it hard for the body to produce enough haemoglobin. Haemoglobin helps the body's red blood cells carry oxygen, and when there isn't enough hemoglobin, the number of red blood cells goes down. This condition is called anaemia.

The main treatment for these diseases is blood transfusion, in which fresh blood cells packed from healthy red blood cells capable of doing their job, is infused into a patient's own blood. However, transfusion produces a significant non-desirable effect: the body is unable to remove the iron contained in the new transfused blood that accumulates in the liver and other organs (heart and endocrine organs) causing several problems. This is called "iron-overload".

Deferiprone is a medicine that has demonstrated good efficacy in reducing iron-overload in the bodies of adults and children over six years with thalassaemia, particularly in the heart. In the DEEP-2 study, researchers wanted to find out if this medicine would be beneficial for use starting from the earliest possible ages and in all transfusion-dependent anaemias. Since children bodies behave differently from adults, it was essential to carefully study before all its effects and verify that it was effective and safe in children of all ages.

How does the studied medicine work?

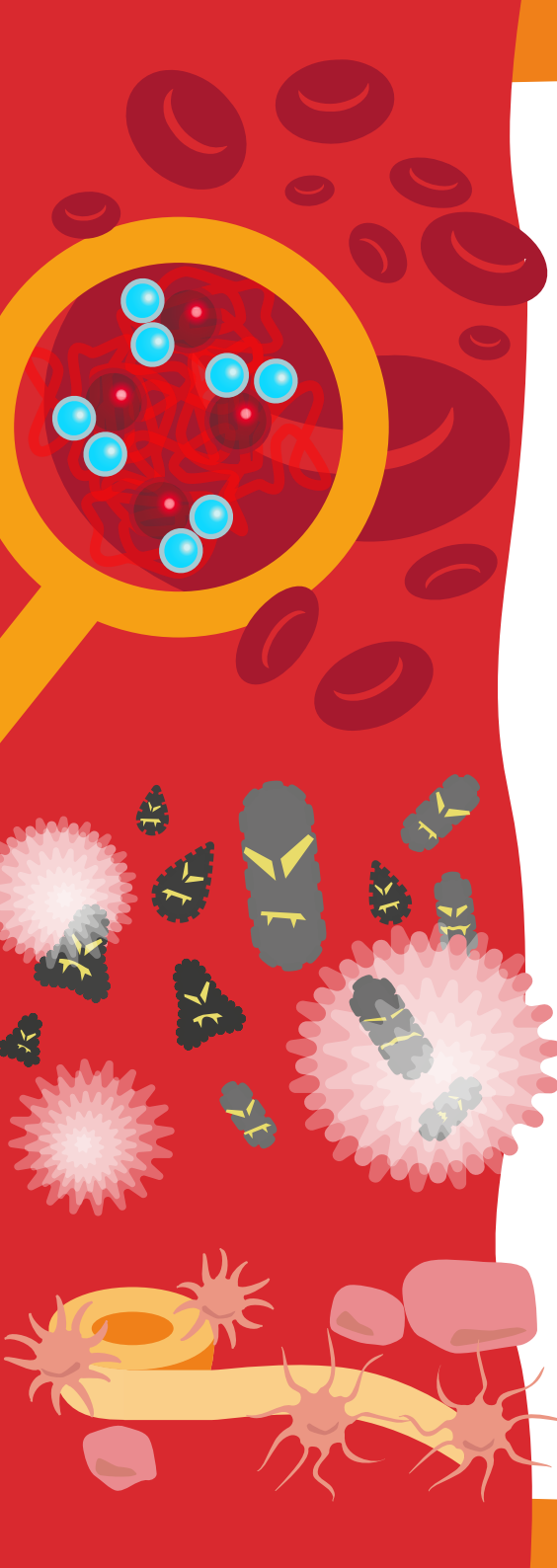
To remove excess iron from the body there are various types of medicines. These medicines act like the claws of a crab: they trap the iron and take it away with them when they are excreted in the urine.

This crab-like treatment using this medicine is known as iron-chelation therapy. Among these medicines, deferiprone is a drug for oral use studied in form of syrup in the DEEP-2 study. To reach strong evidence of the beneficial effects of deferiprone, it was compared to deferasirox, another oral chelator in tablet form that is already being used in children and adolescents needing chelation therapy.

Who has sponsored the DEEP-2 clinical study?

A sponsor is an individual, institution, company or organisation that takes the responsibility to initiate, manage, or finance a clinical study. In the case of the DEEP-2 study, the sponsor was **Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF)**, an organisation that considers it important to share the study's results not only with the general society but also with adolescents and children.

CVBF coordinated the DEEP project and developed this summary in collaboration with **TEDDY European Network of Excellence for Paediatric Research**.



The Components of the Blood

Blood contains lots of substances, such as sugars, fats, vitamins and minerals, and transports millions of cells (i.e. red blood cells, white blood cells and platelets) around our bodies.

Red blood cells (or erythrocytes) account for up to 45% of blood volume, under normal conditions. The bright red colour which gives them their name is due to the presence of haemoglobin, a protein with an iron atom at its heart. When blood passes through the lungs as it travels round the body, each iron atom inside the red blood cells takes up an oxygen molecule. With this precious cargo, the red blood cells then resume their journey, carrying oxygen round the body and releasing it where it is needed. Once it has been released, oxygen becomes our fuel and provides the energy we need for our movements, our thoughts and all our bodily functions, from the simplest to the most complex.

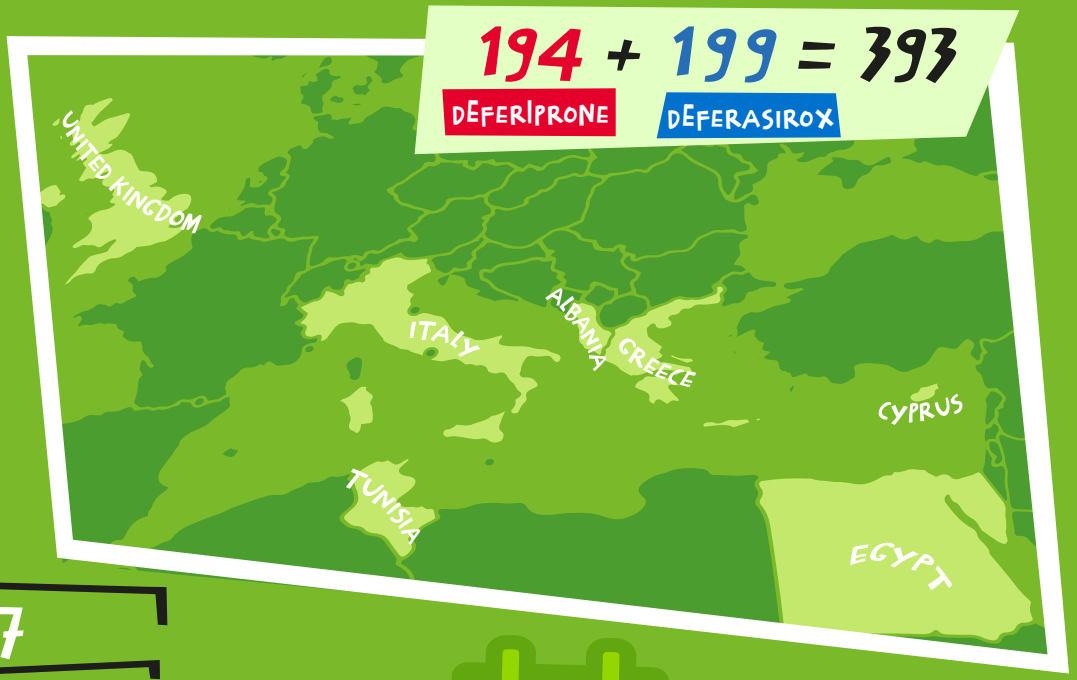
By contrast, less than 1 % of the blood is made up of **white blood cells** (or leukocytes). These cells have a very different, but equally important function: they protect the body against infections and diseases that get into the body, by destroying any bacteria and that get in from outside.

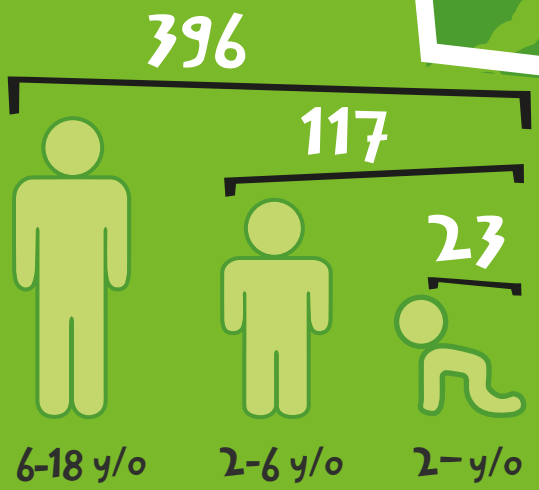
Lastly, a tiny proportion of the blood is made up of **platelets**. These cells help the blood to clot, one of the mechanisms which the body uses to repair itself when it is injured.

Who took part in this study?

The DEEP-2 clinical study was done in children and youths under the age of 18 originating from Albania, Cyprus, Greece, Egypt, Italy, Tunisia, and United Kingdom. In total 393 patients were included all young patients were affected by any hereditary haemoglobinopathies requiring chronic transfusion therapy.

194 patients were treated with deferiprone and 199 with deferasirox. For the first time in a clinical study, also patients younger than 6 years were involved in a trial.



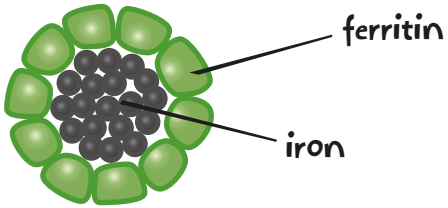


How was this study done?

The 393 patients' participants were divided randomly into two groups. The doctors assigned a different medicine to each group, either deferiprone or deferasirox, and carefully compared their effects, in terms of efficacy and safety.
To evaluate efficacy, researchers and medical doctors checked the quantity of accumulated iron by measuring ferritin level in the blood and using Magnetic Resonance Imaging (MRI) technology in their heart and liver.

Ferritin

is a protein contained in the cells of the human body that circulates in the blood and stores iron, so ferritin is an excellent indicator of the iron quantity in the body (e.g., overload).



Adverse events

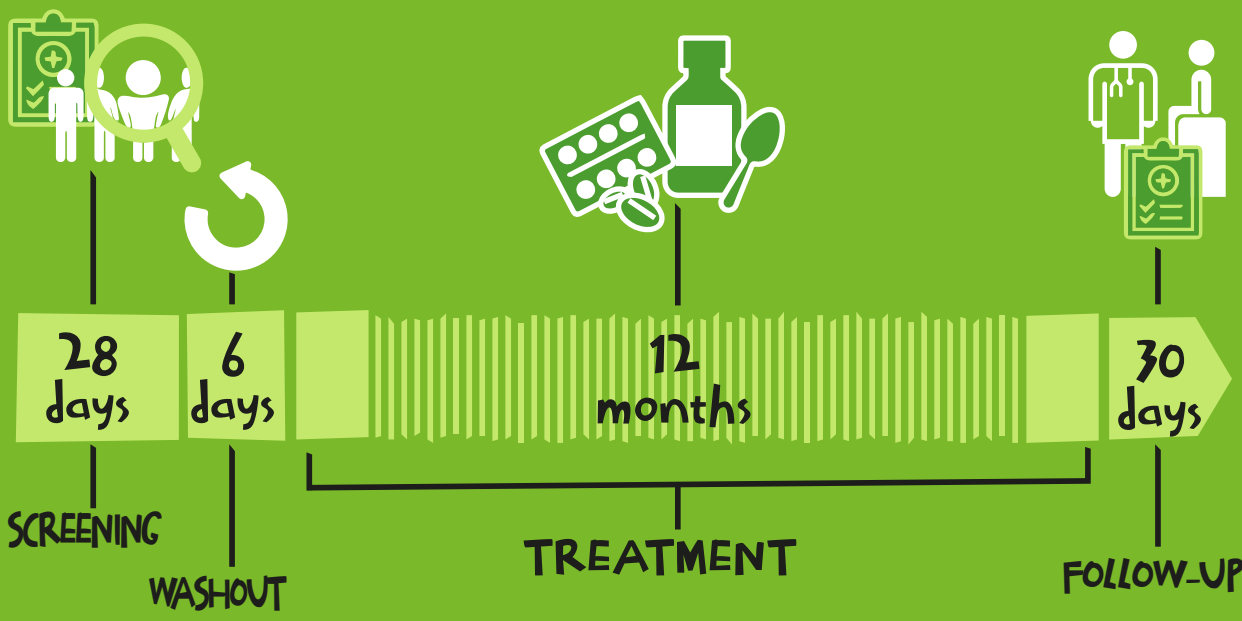
All the medicines that we take have beneficial effects, but sometimes medicines also act on other parts of our body and produce an unwanted medical problem (called **adverse event**).

An adverse event is considered as "serious" if it caused life-threatening condition or if it required the participant to stay in a hospital.

To assess safety, the researchers recorded all unwanted medical problems that happened during the study, including the adverse events related to the treatments and those considered unrelated by doctors.
The goal was to compare improvement in participants who were given deferiprone syrup to those who were given deferasirox soluble tablets after 12 months of treatments.

The study started in March 2014, date of the first patient enrolled, and ended in September 2017, date of the last visit for the last patient.
Each patient participated in the study for a period of approximately 14 months, and went through:

- 28-day screening period, when the doctors selected the participants to the trial
- 6-day washout period, when the participants were asked to discontinue any iron-chelation treatment that they were following up until that point
- 12 months of treatment (with deferiprone or deferasirox)
- 30-day follow-up, when patients were given a final in-depth check-up



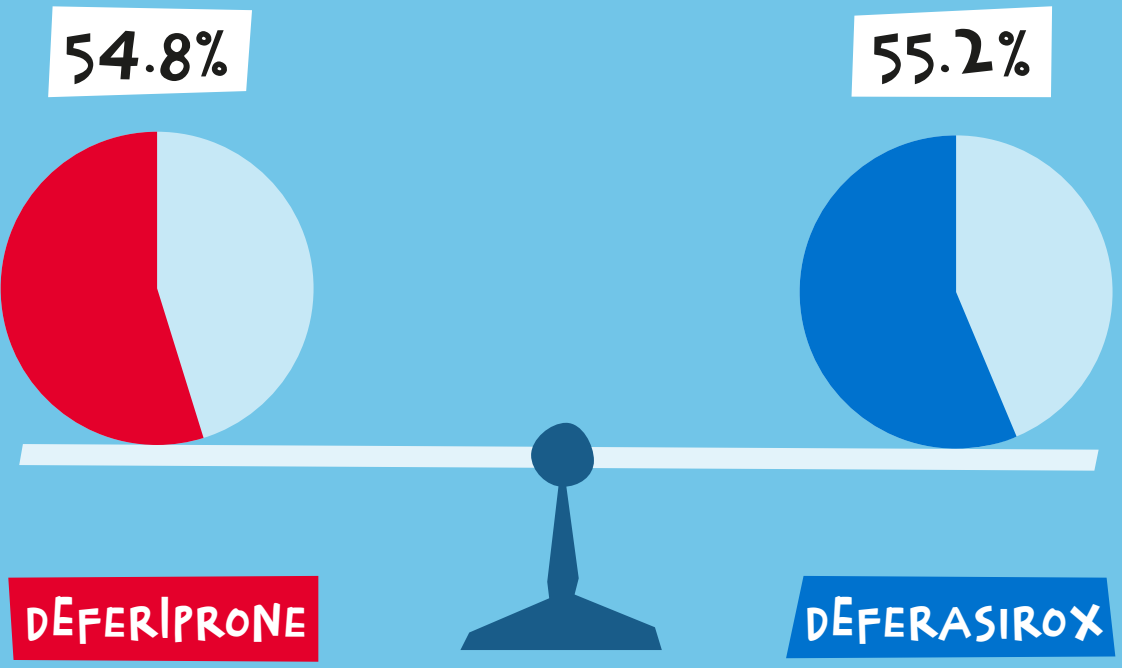
During the trial, all patients regularly got blood samples to measure the ferritin level, white blood cells, and other blood's values.
Of a total of 393 patients involved, 310 patients completed the 12 months treatment. At the end of the treatment period for all patients, researchers compared the effects of the two drugs.

What were the DEEP-2 study results?

The study provided strong evidence that using deferiprone helps improve symptoms in children and adolescents with hereditary haemoglobinopathy who need ongoing blood transfusions.

Is deferiprone efficacious?

The majority of patients treated with deferiprone were successfully chelated and that similar results was obtained in patients treated with deferasirox. The evaluation was performed measuring the reduction of ferritin levels in blood and iron levels in heart and liver by MRI.
In particular, the study demonstrated the effectiveness of chelation in children of every age, even in very young patients.



Is deferiprone safe?

The two medicines used in the DEEP-2 trial had some adverse events, but they were not generally dangerous and only rarely were serious. Some participants had more than one unwanted medical problem over the year of treatment.
The overall number of adverse events was found to be similar in both treatment groups. The number and the seriousness of these events in DEEP-2 did not exceed those experienced in adults.
Certain adverse events, such as diarrhoea, vomiting, and abdominal pain, were similar for the two treatments. In all the cases, these effects diminished over time and did not compromise the patient's wellbeing. Only rarely, especially in case of deferiprone, did patients discontinue their treatments due to abdominal pain and discomfort.
Other adverse events were common like low levels of white blood cells; however, with deferiprone there were very rare cases where this effect was more relevant. For this reason, it is necessary to regularly control white blood cells level.
More joint pain in patients treated with deferiprone and more kidney abnormalities in who's treated with deferasirox were observed.

In conclusions

Finally, the results of the study demonstrated that deferiprone and deferasirox have very similar positive effects, and both can be useful in children at any age, including very young children.
Also, the analysis of adverse events showed that no new or additional risk was reported in children with respect to adults. The number of serious adverse events has been very limited.

Was DEEP-2 study helpful?

Doctors learned a lot more about the safety and efficacy of deferiprone and deferasirox in children and adolescents thanks to DEEP-2.
In particular, they learned about the effects of oral chelators in very young children affected by thalassemia and sickle cell disease and demonstrated that deferiprone may be administered as first chelator alternatively to deferasirox.
If you want to know more about DEEP-2 study, check the project website:

www.deepproject.eu

If you have participated in the study and have questions about its results, doctors or staff at your study site will be able to help you find the answers you need.

This project is founded by the European Union (FP7–GA n° 261483)

DEFERIPRONE EVALUATION IN PAEDIATRICS

CVBF

TEDDY NETWORK
European Network of Excellence for Paediatric Research

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