



## DEEP – DEferiprone Evaluation in Paediatrics



# Presentation



Scientists study every single medicine for a long time before it is given to the general public. The first studies make sure that the medicine is not harmful for the body, while subsequent ones ensure that it does what it is expected to do, with no side effects.

These studies are called “trials” and are carried out under carefully controlled conditions, with all medicines being administered under the supervision of a network of medical experts from many different countries.



The **DEEP-2 trial** will make sure that **deferiprone** is both effective and safe. Deferiprone is a medicine that removes iron overload in kids suffering from diseases such as thalassaemia, sickle cell anaemia and other transfusion-dependent anaemias. This trial is part of a project called DEEP (short for Deferiprone Evaluation in Paediatrics, in other words finding out how deferiprone works in kids) and it has set itself a very important goal. Deferiprone has not been studied much in paediatrics, but if the results of the DEEP-2 trial are positive, all kids like you will be able to use it safely.

When you read  
this booklet,  
you will be able  
to find out:



How **blood** and **red blood cells** work

What **transfusion-dependent anaemias** are

Why **iron builds up in the body** of patients with  
transfusion-dependent anaemia

What treatments **remove iron overload** from the body

What the **DEEP-2 trial** is for

About the various steps in the DEEP-2 trial and any tests that are  
required

After reading the information in this booklet, **you will be able to decide for yourself** whether to take part in the trial. Your doctor can explain even better what happens in each phase of the trial and, together with your parents, will help you think about your choice.

Good luck!



# What is blood?



Blood is one of the most wonderful tools in our body. It's often called the "river of life", because it performs so many functions that are essential to our existence: it carries substances throughout our organism to nourish and defend the body, it removes waste, it keeps us warm and provides substances which help us grow and affect how we behave.

Blood is made up of millions of tiny cells swimming in a liquid called **plasma**.

## What are the components of 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 cell



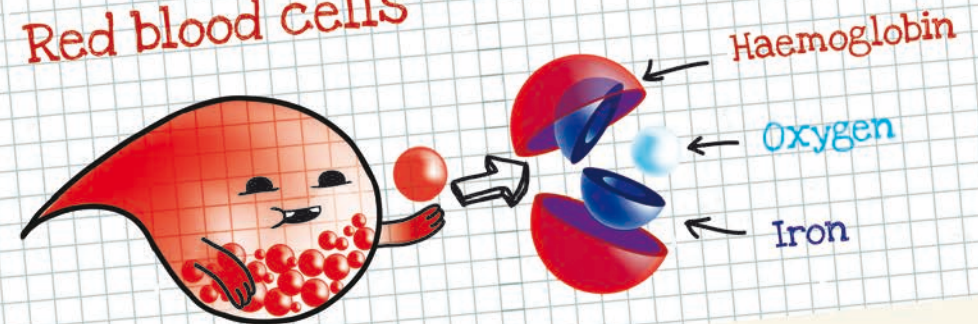
Platelet



White blood cell

**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.

## Red blood cells

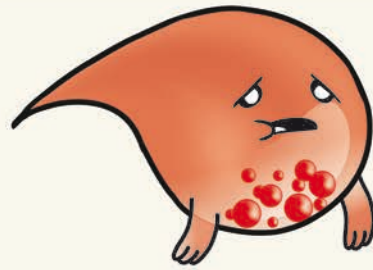


By contrast, less than 1% of the blood is made up of **white blood cells** (or leukocytes). These cells have a very different, but equally important, function: they protect the body against infections and diseases that get into the body, by destroying any bacteria and viruses that get in from outside.

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.



# What are anaemias?



Anaemias are a large family of diseases, all of which affect the blood. They have different causes and mechanisms, but all have the same effect: **they reduce the number of red blood cells**, causing a **haemoglobin deficiency**.

When red blood cells or haemoglobin stop working properly, they can no longer bind oxygen and so cannot transport it around the body. And when there isn't enough oxygen, the tissues can be damaged and cease to function.

From birth, patients with certain inherited diseases such as **beta-thalassaemia major**, **sickle-cell** and other forms of anaemia, have abnormal red blood cells, which are unable to carry out their tasks because of their unusual shape. These patients are at great risk and it is very important to help them as early as possible.

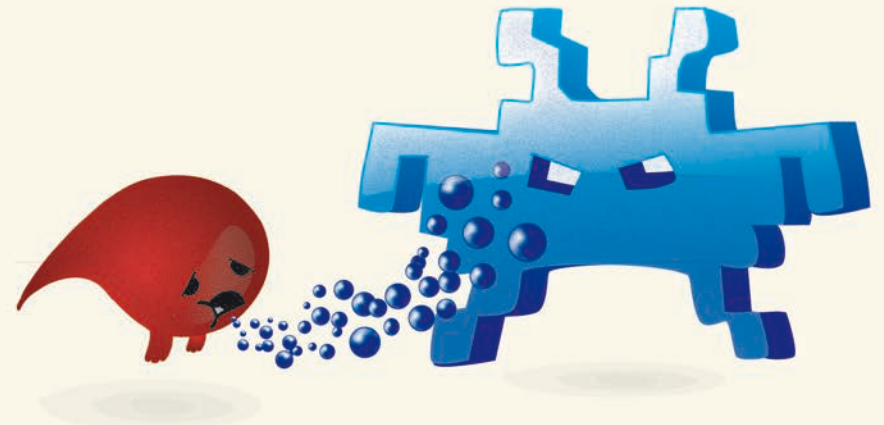
The main treatment for these diseases is **blood transfusion**, in which fresh blood packed with healthy red blood cells capable of doing their job is infused into a patient's own blood. For this reason, anaemias which require blood transfusions are known as **transfusion-dependent anaemias**.



# What are the side effects of blood transfusions?

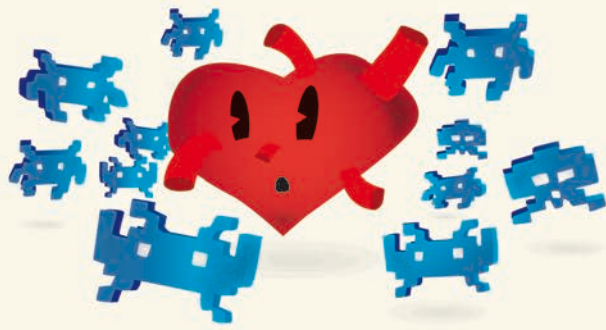
Red blood cells cannot live for ever and are regularly eliminated to make room for new red blood cells. In patients with transfusion-dependent anaemias, red blood cells have an even shorter life expectancy. That explains why a transfusion of healthy blood is needed every 15-20 days. Only recently-transfused blood can transport oxygen and thus enable the patient to enjoy a similar lifestyle to his/her peers.

Transfusion, however, produces a significant side effect. The body is unable to remove the iron atoms contained in the new transfused blood. This iron slowly builds up inside a molecule called **ferritin**.



This so-called "iron overload" can cause several disorders, but the main problems arise in the **heart**, the engine that pumps the blood round the body, and in the **liver**, the regulator of so many mechanisms needed for a healthy body. As time passes, these disorders become serious and dangerous and **must absolutely be prevented**.





## How do we eliminate iron overload?

From a very young age, patients with transfusion-dependent anaemias also take medicines to remove excess iron from the body. 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**.

Iron-chelation therapies use three different drugs that all have the same effect, but work differently in the body.

## What are these iron-chelation therapies?



### Deferoxamine

This medicine is slowly injected into the patient using an electronic pump.



### DeferaSirox

This medicine is taken once a day in the form of a tablet dissolved in water.



### Deferiprone

This medicine is taken three times a day in the form of tablets or syrup. Among the medicines in this group, this is the one that is best at removing iron overload in the heart, but it has not yet been thoroughly studied in children and adolescents.

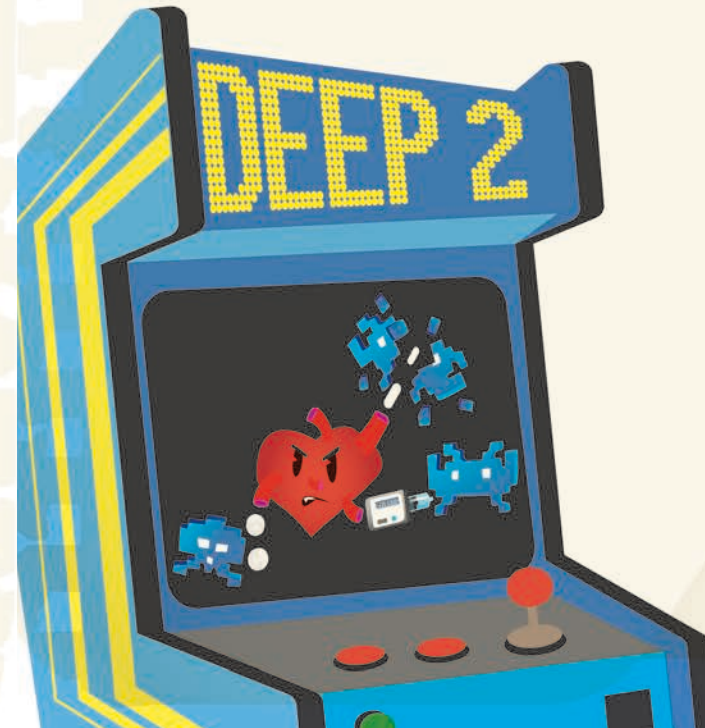
## Which iron-chelation therapy is the best one?

There is no such thing as the perfect treatment. Each patient reacts differently to medication, so it is vital **to have different treatments available**. That is the only way for every patient to get the most suitable therapy for him/her.

## The DEEP-2 clinical trial

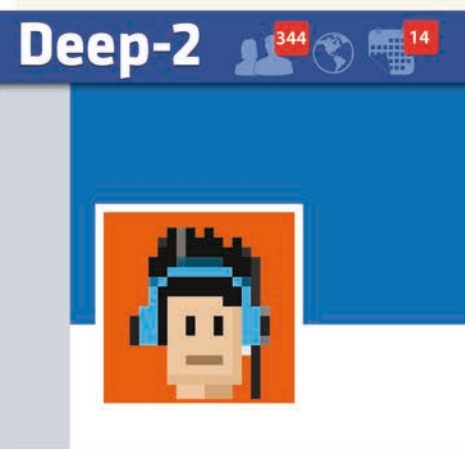
**Deferiprone** has been studied primarily in adult patients with thalassaemia. This medicine has demonstrated good efficacy in removing iron overload in the heart, and doctors would like to use it in all transfusion-dependent anaemias, from the earliest possible age.

It must, however, be remembered that the body of a child or adolescent behaves differently from that of an adult. Before we go ahead and administer this drug widely to children and adolescents, it is vital that we carefully study all its effects on them. This type of research is called a clinical trial or **clinical study**.





## The DEEP-2 clinical trial which we are asking you to take part in is based on a simple mechanism



344 patients from different countries will be divided randomly into two groups of equal size. The process by which patients are randomly drawn out of a hat and assigned to one of the two groups is called **randomisation**. The doctors will assign a different medicine to each group and compare the effects. This will enable us to establish with some degree of certainty whether the new deferiprone syrup is as effective as the deferasirox tablets.



On the basis of this study method, following the randomisation step, patients in the first group will – for a year – take a new deferiprone syrup, which tastes nicer than the current one, while the second group of patients will take the same medicine in the form of soluble tablets (deferasirox), again for a year. The doctors will carefully follow all of the participants on the trial and will check that the medicine has no adverse effects. At the end of the trial, the doctors will compare the two groups and check whether both drugs have worked as expected.

The DEEP-2 clinical trial is designed for children and young people under the age of 18, originating from Italy, Greece, Cyprus, Egypt, Tunisia and Albania. Their participation will help doctors to make sure that the new medicine works perfectly for all ages and in all countries.

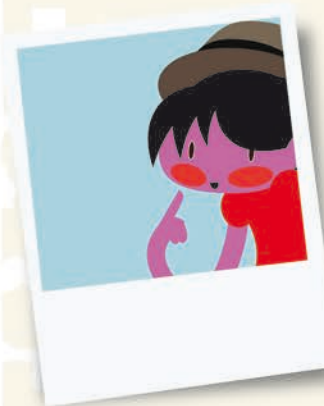
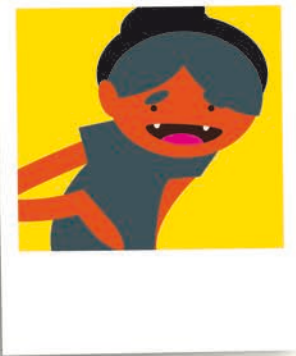


## Is participation in this trial mandatory?

No, taking part in the DEEP-2 trial **is not** mandatory. Each young patient can decide freely whether or not to participate in the trial. Parents will need to approve their child's decision. Every patient who decides not to participate in the trial will continue to be treated in the same way as before and will still receive the full attention of his/her doctors.

## Can I leave the trial once it has begun?

Any patient who wishes to do so may leave the trial at any time, without having to give any explanation. He/she will be treated with the chelation therapy best suited to him/her and will continue to receive the full attention of doctors.



## Is deferiprone treatment safe?

Like any therapy, deferiprone also has side effects that are usually mild and well known to the doctors running the trial. In order to ensure maximum safety, however, doctors will continually monitor all trial participants and could, if necessary, discontinue treatment.

Furthermore, the effects of these medicines on unborn babies have not yet been studied. Pregnancy should therefore be avoided. If a patient does become pregnant, the doctor should be informed immediately.





Your route,  
step by step



Syrup



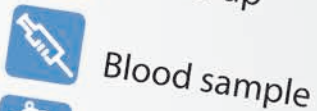
Tablets



Electrocardiogram



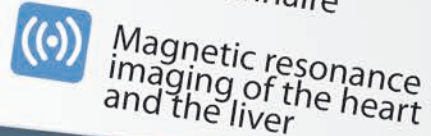
Check-up



Blood sample



Questionnaire



Magnetic resonance  
imaging of the heart  
and the liver





## What will happen during the DEEP-2 trial?

The DEEP-2 trial itself lasts a total of 14 months, but the treatment will last 12 months.

The **month before starting treatment**, the doctors will select the participants.

In the **6 days before** starting treatment, participants will be asked to discontinue the iron-chelation treatment that they were following up until that point.

That way, the body will get rid of all traces of the previous medicine, so that it can't affect how the study medicine works.

During the **first day of treatment**, the 344 patients will be assigned to the deferiprone group (syrup) or to the deferasirox group (soluble tablets).

From that moment onwards, patients assigned to the deferiprone group will take the syrup three times daily after meals, while patients assigned to the deferasirox group will take the tablets once a day on an empty stomach.

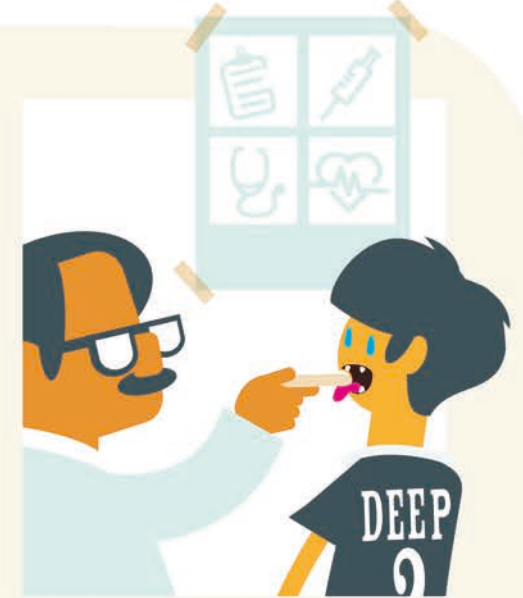
In addition, some patients will fill out questionnaires, will have a blood sample taken, and will have an electrocardiogram (ECG).

At the end of the **twelfth month of treatment**, patients will discontinue treatment and will have the final tests (blood sample, in-depth check-up, electrocardiogram, heart and liver magnetic resonance imaging).

One **month after the end of treatment**, patients will be given a final in-depth check-up.



## What will happen at the monthly visits during the trial?



During the monthly visits, the doctor will make sure that participants are feeling well.

The **blood samples** will be used to check that the participants are in good health and that their kidneys and liver are in good condition. As blood counts will be continuously monitored, the trial will be completely safe. The blood samples will also be used to check:



the amount of **ferritin**, which corresponds to the amount of iron in the body; during the trial this quantity must either decrease (if it is too high) or stay constant (if it is already at an acceptable level).



the amount of **white blood cells**, these cells are very important for defending the body and must not decrease during the trial.







**Electrocardiogram (ECG)** is a short and simple test used to record the heart's electrical activity and make sure it is working properly.

**Heart and liver magnetic resonance imaging (MRI)** are two very important tests. They enable a computer to recreate an image of the heart and liver, so that the doctor can check whether the medicine is working or whether there is any iron overload. At the beginning of the examination, the patient will lie down on a bed which will then slide into a tube-shaped machine. The machine will then explore the patient's organs using a magnetic field and radio waves and will then send all the data back to the central computer. Like all of the examinations in the DEEP-2 trial, MRI is neither painful nor dangerous. It only takes a bit of patience: the patient has to stay inside the machine for about 20 minutes following the doctor's instructions.



## Undesirable effects

All the medicines that we take for their beneficial effects can sometimes also act on other parts of our body and produce side effects. Even the two medicines used in the DEEP-2 trial can produce some of these effects, but they are not generally dangerous.

During treatment, the patient may experience a reduction in **white blood cells**, a reduction in **platelets**, and **liver** or **kidney** disorders. The doctors will take a blood sample every week to check that these effects do not occur.

### There are other less significant side effects:

- gastrointestinal disturbances (nausea, vomiting, diarrhoea)
- pain in arms or legs
- itching
- skin irritation
- change in urine colour

Remember that these effects are not usually dangerous, but it is important **to tell your doctor immediately** if you get any disorder. Your doctor will decide whether to carry on with the treatment or whether it needs to be discontinued.





# Frequently Asked Questions

## What are these iron-chelation therapies?

These are medicine-based treatments that reduce the iron overload in patients who have frequent transfusions, such as people suffering from anaemia. Iron overload is very dangerous for your health and you must prevent it.



## What iron-chelation therapies are available?

Current treatments use deferoxamine (injected into the patient using an electronic pump), deferasirox (tablets to dissolve in water) and deferiprone (tablets or syrup).

## What is the perfect iron-chelation therapy?

There is not such thing as a perfect therapy, because each of us responds differently to medicines. So it's important to have several treatments available.

## What is the DEEP-2 trial for?

Deferiprone is very good at removing iron overload from the heart and is an effective iron-chelation treatment. The DEEP-2 trial will examine the effects of deferiprone in the youngest thalassaemia patients and in all young patients with other types of transfusion-dependent anaemia, in which the effects of deferiprone are still poorly understood.



## Is the DEEP-2 trial safe?

During the DEEP-2 trial, each participant will be closely followed by his/her doctor and their health will always be monitored.



## Do I have to take part in the DEEP-2 trial?

No, taking part in the DEEP-2 trial is not mandatory and you must not feel at all forced into taking part. Everyone will respect your decision and your doctor will continue to treat you just like before.

## Can I leave the DEEP-2 trial?

If you no longer wish to participate in the trial, all you need to do is inform your doctor. You will start taking the old treatment again and your doctor will continue to treat you just like before.

## What happens if I miss a dose of Syrup or a tablet?

Make sure you take all the doses on schedule. However, if you do miss one, don't worry. Remember to let your doctor know as soon as possible and keep taking the syrup or tablets as usual.

## What will happen if I get any undesirable effects?

Alert your doctor immediately. Undesirable effects are generally not dangerous, but your doctor will decide if you can continue to take part in the trial or if you need to go back to your old treatment.

## What makes the DEEP-2 trial important?

Deferiprone can be a very effective drug and useful for all young people with transfusion-dependent anaemias. By participating in the DEEP-2 trial, you will be helping doctors to decide whether this medicine can also be used for them. And by doing so, you will be helping many other young people like you.



## Protection of privacy and personal data

The personal data of trial participants will be treated with the strictest confidentiality and shall not be disclosed to anyone outside of the doctors and close family members.

By law (European Directive 1995/46/EC on data confidentiality), all those involved in the trial have an obligation to use all the means at their disposal to ensure that any information about you and your condition is kept confidential and that nobody can trace you through the information that is collected about you, except your doctor and the people he/she has entrusted to take care of you.

All persons involved in the trial are bound by professional secrecy.

The data will be used anonymously to inform the Ethics Committees and the domestic and European health authorities.

You are entitled to know the results of the trial, both general ones and those that directly concern you.

Once the trial is completed, the results will be made available to the public, published in a medical journal or presented at a scientific conference. In any case, any information will be disclosed anonymously and no participants in the trial will be identifiable.



# DEEP

## DEferiprone Evaluation in Paediatrics

Funded by the European Commission under the 7th Framework Programme  
(FP7 Project - SP1 - Cooperation HEALTH-F4-2010-261483)

### Study Title:

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

### Clinical Study DEEP-2

EudraCT number: 2012-000353-31

Consorzio per Valutazioni  
Biologiche e Farmacologiche

Scientific Coordinator  
Adriana Ceci

Project Manager  
Donato Bonifazi

Scientific Team  
Aurelio Maggio  
Paola Baiardi  
Mohamed Bejaoui  
Amal El-Beshlawy  
Soteroula Christou  
Giancarlo Del Vecchio  
Slaheddine Fattoum  
Aldo Filosa  
Antonis Kattamis  
Manika Kreka  
Laura Mangiarini  
Caterina Putti

Booklet production coordinator  
Maria Cavallo

Content editor  
Leonardo Rizzi

Illustrations and Graphic Design  
Claudio Cazzolino

Translation co-ordinator  
Anthony Green

